			the invention (including	and hematonoietic disorders
			antihodies and agonists or	(e σ as described helow under
			antogonists of the invention) to	"Immine Activity" and
			annagomets of the invention) to	initialist Activity, and
			regulate viability and	"Blood-Related Disorders"),
			proliferation of eosinophil cells	autoimmune diseases (e.g.,
			and cell lines. For example,	rheumatoid arthritis, systemic
			the CellTiter-Gloô	lupus erythematosis, Crohn"s
			Luminescent Cell Viability	disease, multiple sclerosis
 			Assay (Promega Corp.,	and/or as described below),
			Madison, WI, USA) can be	immunodeficiencies (e.g., as
			used to measure the number of	described below). Highly
			viable cells in culture based on	preferred indications also
			quantitation of the ATP	include boosting or inhibiting
			present which signals the	immune cell proliferation.
			presence of metabolically	Preferred indications include
			active cells. Eosinophils are a	neoplastic diseases (e.g.,
			type of immune cell important	leukemia, lymphoma, and/or as
			in allergic responses; they are	described below under
			recruited to tissues and	"Hyperproliferative
			mediate the inflammtory	Disorders"). Highly preferred
			response of late stage allergic	indications include boosting an
			reaction. Eosinophil cell lines	eosinophil-mediated immune
			that may be used according to	response, and suppressing an
			these assays are publicly	eosinophil-mediated immune
 			available and/or may be	response.
			routinely generated.	
			Exemplary eosinophil cells	
			that may be used according to	
			these assays include EOL-1	
	!		Cells.	
НDРВQ71	1053	Production of	IFNgamma FMAT. IFNg plays	A highly preferred

mune   embodiment of the invention	ed to be includes a method for	okine. stimulating the production of		ation; preferred embodiment of the	hibits invention includes a method	for inhibitin		indications	dulatory   disorders (e.g., as described	<u> </u>	late a   Activity", "Blood-Related	y Disorders", and/or		re well and infection (e.g., viral	nay be infections, tuberculosis,		chronic granulomatosus	rention disease and malignant	ind osteoporosis, and/or as	of the described below under		gulate preferred indications include		cell rheumatoid arthritis, systemic		ted sclerosis and/or as described		(e.g., as described below),		
IFNgamma using a a central role in the immune	system and is considered to be	a proinflammatory cytokine.	IFNg promotes TH1 and	inhibits TH2 differentiation;	promotes IgG2a and inhibits	IgE secretion; induces	macrophage activation; and	increases MHC expression.	Assays for immunomodulatory	proteins produced by T cells	and NK cells that regulate a	variety of inflammatory	activities and inhibit TH2	helper cell functions are well	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, regulate	inflammatory activities,	modulate TH2 helper cell	function, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays	that test for	immunomodulatory proteins	
IFNga	T cells														~~~											-				_
105			•																											_

	cytokines, such as Interferon	suppressing a T cell-mediated
	gamma (IFNg), and the	immune response. Additional
	activation of T cells. Such	highly preferred indications
	assays that may be used or	include inflammation and
	routinely modified to test	inflammatory disorders.
	immunomodulatory activity of	Additional preferred
	polypeptides of the invention	indications include idiopathic
	(including antibodies and	pulmonary fibrosis. Highly
	agonists or antagonists of the	preferred indications include
	invention) include the assays	neoplastic diseases (e.g.,
	disclosed in Miraglia et al., J	leukemia, lymphoma,
	Biomolecular Screening 4:193-	melanoma, and/or as described
	204 (1999); Rowland et al.,	below under
	"Lymphocytes: a practical	"Hyperproliferative
	approach" Chapter 6:138-160	Disorders"). Highly preferred
	(2000); Gonzalez et al., J Clin	indications include neoplasms
	Lab Anal 8(5):225-233 (1995);	and cancers, such as, for
	Billiau et al., Ann NY Acad	example, leukemia, lymphoma,
	Sci 856:22-32 (1998); Boehm	melanoma, and prostate,
	et al., Annu Rev Immunol	breast, lung, colon, pancreatic,
	15:749-795 (1997), and	esophageal, stomach, brain,
	Rheumatology (Oxford)	liver and urinary cancer. Other
	38(3):214-20 (1999), the	preferred indications include
	contents of each of which are	benign dysproliferative
	herein incorporated by	disorders and pre-neoplastic
	reference in its entirety.	conditions, such as, for
	Human T cells that may be	example, hyperplasia,
	used according to these assays	metaplasia, and/or dysplasia.
	may be isolated using	Preferred indications include
	techniques disclosed herein or	anemia, pancytopenia,
	otherwise known in the art.	leukopenia, thrombocytopenia,

				Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cellmediated immunity and may	Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia,
				be preactivated to enhance responsiveness to immunomodulatory factors.	neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
106	HDPCJ91	1054	Activation of Skeletal Mucle Cell PI3 Kinase Signalling Pathway	Kinase assay. Kinase assays, for example an GSK-3 kinase assay, for PI3 kinase signal transduction that regulate glucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of	A highly preferred embodiment of the invention includes a method for increasing muscle cell survival An alternative highly preferred embodiment of the invention includes a method for decreasing muscle cell survival. A preferred
				the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for PI3 kinase activity that may be	embodiment of the invention includes a method for stimulating muscle cell proliferation. In a specific embodiment, skeletal muscle cell proliferation is stimulated. An alternative highly preferred

embodiment of the invention includes a method for inhibiting muscle cell	proliferation. In a specific embodiment, skeletal muscle	cell proliferation is inhibited.  A preferred embodiment of	the invention includes a	method for stimulating muscle	specific embodiment, skeletal	muscle cell differentiation is	stimulated. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting muscle	cell differentiation. In a	specific embodiment, skeletal	muscle cell differentiation is	inhibited. Highly preferred	indications include disorders of	the musculoskeletal system.	Preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), endocrine	disorders (e.g., as described	below under "Endocrine	Disorders"), neural disorders	le o as described below under
used or routinely modified to test PI3 kinase-induced activity of polypeptides of the	invention (including antibodies and agonists or antagonists of	the invention) include assays disclosed in Forrer et al., Biol	Chem 379(8-9):1101-1110	(1998); Nikoulina et al.,	(2000); and Schreyer et al.,	Diabetes 48(8):1662-1666	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Rat myoblast cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary rat myoblast cells	that may be used according to	these assays include L6 cells.	L6 is an adherent rat myoblast	cell line, isolated from primary	cultures of rat thigh muscle,	that fuses to form	multinucleated myotubes and	striated fibers after culture in	differentiation media.		
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"Neural Activity and	Neurological Diseases"), blood	disorders (e.g., as described	below under "Immune	Activity", "Cardiovascular	Disorders", and/or "Blood-	Related Disorders"), immune	disorders (e.g., as described	below under "Immune	Activity"), and infection (e.g.,	as described below under	"Infectious Disease"). A	highly preferred indication is	diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage (e.g.	due to diabetic neuropathy),	blood vessel blockage, heart	disease, stroke, impotence	(e.g., due to diabetic	lassed booth or blood wessel

blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infections	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include
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or alterr	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal system	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include: myopathy,	atrophy, congestive heart	failure, cachexia, myxomas,	fibromas, congenital	cardiovascular abnormalities,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease. Highly	preferred indications include	neoplasms and cancer, such as,	rhabdomyoma,	rhabdosarcoma, stomach,	esophageal, prostate, and	urinary cancer. Preferred	indications also include breast,	lung, colon, pancreatic, brain,	and liver cancer. Other	preferred indications include	benign dysproliferative
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					disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.
107	HDPC025	1055	Regulation of viability and proliferation of	Assays for the regulation of viability and proliferation of cells in vitro are well-known in	A highly preferred indication is diabetes mellitus. An additional highly preferred
			pancreatic beta cells.	the art and may be used or routinely modified to assess the ability of polypeptides of	indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic
				the invention (including antibodies and agonists or	nephropathy, kidney disease (e.g., renal failure,
				antagonists of the invention) to regulate viability and	diseases and disorders as
				cells. For example, the Cell	Disorders" section below),
	· · · · · · · · · · · · · · · · · · ·			Titer-Glo luminescent cell viability assay measures the	diabetic neuropathy, nerve disease and nerve damage
			,	number of viable cells in culture based on quantitation	(e.g., due to diabetic neuropathy), blood vessel
				of the ATP present which signals the presence of	blockage, heart disease, stroke, impotence (e.g., due to diabetic
				metabolically active cells. Exemplary assays that may be	neuropathy or blood vessel blockage), seizures, mental
				used or routinely modified to	confusion, drowsiness,
				test regulation of viability and proliferation of pancreatic beta	nonketotic hyperglycemic- hyperosmolar coma,
				cells by polypeptides of the invention (including antibodies	cardiovascular disease (e.g.,
				and agonists or antagonists of	microvascular disease,
				the invention) include assays	hypertension, stroke, and other

				Natl. Acad. Sci. USA 78:	
		-		4339-4343, 1981.	
:	HDPC025	1055	Activation of	Assays for the activation of	Highly preferred indications
107			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as T-cells).	to assess the ability of	as described below under
				polypeptides of the invention	"Immune Activity", "Blood-
				(including antibodies and	Related Disorders", and/or
				agonists or antagonists of the	"Cardiovascular Disorders").
				invention) to regulate NFKB	Highly preferred indications
				transcription factors and	include autoimmune diseases
				modulate expression of	(e.g., rheumatoid arthritis,
•				immunomodulatory genes.	systemic lupus erythematosis,
				Exemplary assays for	multiple sclerosis and/or as
				transcription through the	described below), and
				NFKB response element that	immunodeficiencies (e.g., as
·				may be used or rountinely	described below). An
	_			modified to test NFKB-	additional highly preferred
		4.4		response element activity of	indication is infection (e.g.,
				polypeptides of the invention	AIDS, and/or an infectious
				(including antibodies and	disease as described below
				agonists or antagonists of the	under "Infectious Disease").
				invention) include assays	Highly preferred indications
-tu				disclosed in Berger et al., Gene	include neoplastic diseases
				66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
				Malm, Methods in Enzymol	lymphoma, and/or as described
				216:362-368 (1992); Henthorn	below under
			·	et al., Proc Natl Acad Sci USA	"Hyperproliferative
				85:6342-6346 (1988); Black et	Disorders"). Highly preferred

indications include neoplasms and cancers, such as,melanoma, renal cell carcinoma, leukemia, lymphoma, and prostate,	breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for	example, nyperplasta, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma,	arthritis, ALDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted
al., Virus Gnes 15(2):105-117 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by	reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary human T cells that may be used according to these	assays include the SUFT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	

					organs, asthma and allergy.
	HDPCY37	1056	Activation of	Assays for the activation of	A highly preferred indication
108			transcription	transcription through the	is obesity and/or complications
			through cAMP	cAMP response element are	associated with obesity.
			response element	well-known in the art and may	Additional highly preferred
·			(CRE) in pre-	be used or routinely modified	indications include weight loss
			adipocytes.	to assess the ability of	or alternatively, weight gain.
				polypeptides of the invention	An additional highly preferred
A				(including antibodies and	indication is diabetes mellitus.
				agonists or antagonists of the	An additional highly preferred
	2			invention) to increase cAMP,	indication is a complication
				regulate CREB transcription	associated with diabetes (e.g.,
				factors, and modulate	diabetic retinopathy, diabetic
				expression of genes involved	nephropathy, kidney disease
				in a wide variety of cell	(e.g., renal failure,
				functions. For example, a	nephropathy and/or other
				3T3-L1/CRE reporter assay	diseases and disorders as
				may be used to identify factors	described in the "Renal
				that activate the cAMP	Disorders" section below),
				signaling pathway. CREB	diabetic neuropathy, nerve
				plays a major role in	disease and nerve damage
·	-			adipogenesis, and is involved	(e.g., due to diabetic
				in differentiation into	neuropathy), blood vessel
	-			adipocytes. CRE contains the	blockage, heart disease, stroke,
				binding sequence for the	impotence (e.g., due to diabetic
				transcription factor CREB	neuropathy or blood vessel
				(CRE binding protein).	blockage), seizures, mental
				Exemplary assays for	confusion, drowsiness,
				transcription through the	nonketotic hyperglycemic-
				cAMP response element that	hyperosmolar coma,
				may be used or routinely	cardiovascular disease (e.g.,

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heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	Additional highly preferred	indications are complications	associated with insulin	resistance.	,					
modified to test cAMP-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Reusch	et al., Mol Cell Biol	20(3):1008-1020 (2000); and	Klemm et al., J Biol Chem	273:917-923 (1998), the	contents of each of which are	herein incorporated by	reference in its entirety. Pre-	adipocytes that may be used	according to these assays are	publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3
						-																	-							

				fibroblast cells developed through clonal isolation and	
				undergo a pre-adipocyte to	
				appropriate differentiation	
-				conditions known in the art.	
H 108	HDPCY37	1056	SEAP in OE-33		
H	HDPCY37	1056	Activation of	Assays for the activation of	Highly preferred indications
108			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as T-cells).	to assess the ability of	as described below under
				polypeptides of the invention	"Immune Activity", "Blood-
				(including antibodies and	Related Disorders", and/or
<u>.                                    </u>				agonists or antagonists of the	"Cardiovascular Disorders").
				invention) to regulate NFKB	Highly preferred indications
				transcription factors and	include autoimmune diseases
				modulate expression of	(e.g., rheumatoid arthritis,
	-			immunomodulatory genes.	systemic lupus erythematosis,
				Exemplary assays for	multiple sclerosis and/or as
				transcription through the	described below), and
				NFKB response element that	immunodeficiencies (e.g., as
				may be used or rountinely	described below). An
				modified to test NFKB-	additional highly preferred
				response element activity of	indication is infection (e.g.,
				polypeptides of the invention	AIDS, and/or an infectious
				(including antibodies and	disease as described below
				agonists or antagonists of the	under "Infectious Disease").
				invention) include assays	Highly preferred indications

		disclos	disclosed in Berger et al Gene	include neoplastic diseases
		66:1-1		(e.g., melanoma, leukemia,
		Malm,	Malm, Methods in Enzymol	lymphoma, and/or as described
		216:36	216:362-368 (1992); Henthorn	below under
		et al., I	et al., Proc Natl Acad Sci USA	"Hyperproliferative
		85:634	85:6342-6346 (1988); Black et	Disorders"). Highly preferred
		al., Vir	al., Virus Gnes 15(2):105-117	indications include neoplasms
		(1997)	(1997); and Fraser et al.,	and cancers, such
		3:(2):8	29(3):838-844 (1999), the	as,melanoma, renal cell
		conten	contents of each of which are	carcinoma, leukemia,
		herein	herein incorporated by	lymphoma, and prostate,
		referen	reference in its entirety. T	breast, lung, colon, pancreatic,
		cells th	cells that may be used	esophageal, stomach, brain,
		accord	according to these assays are	liver and urinary cancer. Other
		public	publicly available (e.g.,	preferred indications include
		through	through the ATCC).	benign dysproliferative
		Exemp	Exemplary human T cells that	disorders and pre-neoplastic
		may be	may be used according to these	conditions, such as, for
		assays	assays include the SUPT cell	example, hyperplasia,
		line, w	line, which is a suspension	metaplasia, and/or dysplasia.
		culture	culture of IL-2 and IL-4	Preferred indications also
		respon	responsive T cells.	include anemia, pancytopenia,
				leukopenia, thrombocytopenia,
	<u>.</u>			Hodgkin's disease, acute
				lymphocytic anemia (ALL),
				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
				arthritis, AIDS,
				granulomatous disease,
		<u> </u>		inflammatory bowel disease,
-				sepsis, neutropenia,

					neutrophilia, psoriasis,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					suppression of immune
					reactions to transplanted
					organs, asthma and allergy.
	HDPCY37	1056	Production of IL-10	Assays for production of IL-10	Highly preferred indications
108			and activation of T-	and activation of T-cells are	include allergy and asthma.
			cells.	well known in the art and may	Additional highly preferred
				be used or routinely modified	indications include immune
				to assess the ability of	and hematopoietic disorders
			<b>)</b> ,	polypeptides of the invention	(e.g., as described below under
				(including antibodies and	"Immune Activity", and
				agonists or antagonists of the	"Blood-Related Disorders"),
				invention) to stimulate or	autoimmune diseases (e.g.,
				inhibit production of IL-10	rheumatoid arthritis, systemic
				and/or activation of T-cells.	lupus erythematosis, Crohn"s
				Exemplary assays that may be	disease, multiple sclerosis
				used or routinely modified to	and/or as described below),
				assess the ability of	immunodeficiencies (e.g., as
				polypeptides and antibodies of	described below), boosting a T
				the invention (including	cell-mediated immune
			-	agonists or antagonists of the	response, and suppressing a T
				invention) to modulate IL-10	cell-mediated immune
				production and/or T-cell	response.
				proliferation include, for	
				example, assays such as	
				disclosed and/or cited in:	
				Robinson, DS, et al., "Th-2	
				cytokines in allergic disease"	

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11DDEDOO 1057 Assissing of This seasons magazine Highly mafamad indications

			66:1-10 (1998). Cullen and	Disorders") Other preferred
			Molm Mothodo in Engrisol	indications include hearies
-			Iviaini, ivietilous in Elizyiiloi	indications include beingin
			216:362-368 (1992); Henthorn	dysproliferative disorders and
			et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
			85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
			et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
,			Quant Biol 64:563-571 (1999);	Preferred indications include
	-		Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
			J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
			(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
-			Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
			Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
			14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
			contents of each of which are	lymphoma, arthritis, AIDS,
			herein incorporated by	granulomatous disease,
			reference in its entirety. Mast	inflammatory bowel disease,
			cells that may be used	sepsis, neutropenia,
			according to these assays are	neutrophilia, psoriasis,
			publicly available (e.g.,	suppression of immune
			through the ATCC).	reactions to transplanted
			Exemplary human mast cells	organs and tissues, hemophilia,
	- 4 - <del>-</del>		that may be used according to	hypercoagulation, diabetes
			these assays include the HMC-	mellitus, endocarditis,
			1 cell line, which is an	meningitis, and Lyme Disease.
			immature human mast cell line	
	-		established from the peripheral	
	<u></u>		blood of a patient with mast	
			cell leukemia, and exhibits	
			many characteristics of	
			immature mast cells.	
HDPFB02	1057	Production of	Endothelial cells, which are	Highly preferred indications

109		ICAM in	cells that line blood vessels,	include inflammation (acute
		endothelial cells	and are involved in functions	and chronic), restnosis,
		such as human	that include, but are not limited	atherosclerosis, asthma and
	-	umbilical vein	to, angiogenesis, vascular	allergy. Highly preferred
		endothelial cells	permeability, vascular tone,	indications include
		(HUVEC))	and immune cell extravasation.	inflammation and
			Exemplary endothelial cells	inflammatory disorders,
			that may be used in ICAM	immunological disorders,
			production assays include	neoplastic disorders (e.g.
			human umbilical vein	cancer/tumorigenesis), and
			endothelial cells (HUVEC),	cardiovascular disorders (such
	-		and are available from	as described below under
			commercial sources. The	"Immune Activity", "Blood-
			expression of ICAM (CD54),a	Related Disorders",
			intergral membrane protein,	"Hyperproliferative Disorders"
			can be upregulated by	and/or "Cardiovascular
			cytokines or other factors, and	Disorders"). Highly preferred
			ICAM expression is important	indications include neoplasms
			in mediating immune and	and cancers such as, for
		-	endothelial cell interactions	example, leukemia, lymphoma,
			leading to immune and	melanoma, renal cell
			inflammatory responses.	carcinoma, and prostate,
			Assays for measuring	breast, lung, colon, pancreatic,
			expression of ICAM-1 are	esophageal, stomach, brain,
			well-known in the art and may	liver and urinary cancer. Other
			be used or routinely modified	preferred indications include
			to assess the ability of	benign dysproliferative
	-		polypeptides of the invention	disorders and pre-neoplastic
			(including antibodies and	conditions, such as, for
			agonists or antagonists of the	example, hyperplasia,
			invention) to regulate ICAM-1	metaplasia, and/or dysplasia.

expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Rolfe BE, et al., Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365 (1995); and, Grunstein MM, et al., Am J Physiol Lung Cell Mol Physiol, 278(6):L1154- L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety.	Activation of T-  Kinase assay. JNK and p38  Cell p38 or JNK  kinase assays for signal  Signaling Pathway. transduction that regulate cell  proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of antibodies and agonists or antagonists of the invention) to e.g., an infectious disease as promote or inhibit immune cell "Infectious Disease"). Highly preferred indications include
	1058 Activ Cell p Signa
	HDPFF39
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lupus erythematosis, multiple sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below). Additional	highly preferred indications include inflammation and	inflammatory disorders. Highly preferred indications	also include neoplastic	diseases (e.g., leukemia,	lymphoma, and/or as described	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for		metaplasia, and/or dysplasia.	Preferred indications include	arthritis, asthma, AIDS,	allergy, anemia, pancytopenia,	leukopenia, thrombocytopenia,
used or routinely modified to test JNK and p38 kinase-induced activity of	polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include the assays	disclosed in Forrer et al., Biol	(1998); Gupta et al., Exp Cell	Res 247(2): 495-504 (1999);	Kyriakis JM, Biochem Soc	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension-culture	cell line with cytotoxic	activity.
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Hodgkin"s disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt"s lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of imnune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	ρη Si
	Reporter Assay: construct contains regulatory and coding sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its
	Inhibition of squalene synthetase gene transcription.
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	HDPFF39
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				entirety.	
	HDPFP29	1059	Myoblast cell	Assays for muscle cell	Highly preferred indications
1111			proliferation	proliferation are well known in	include diabetes, myopathy,
				the art and may be used or	muscle cell atrophy, cancers of
				routinely modified to assess	muscle (such as,
				the ability of polypeptides of	rhabdomyoma, and
				the invention (including	rhabdosarcoma),
				antibodies and agonists or	cardiovascular disorders (such
				antagonists of the invention) to	as congestive heart failure,
				stimulate or inhibit myoblast	cachexia, myxomas, fibromas,
				cell proliferation. Exemplary	congenital cardiovascular
				assays for myoblast cell	abnormalities, heart disease,
				proliferation that may be used	cardiac arrest, heart valve
				or routinely modified to test	disease, vascular disease, and
				activity of polypeptides and	also as described below under
				antibodies of the invention	"Cardiovascular Disorders"),
				(including agonists or	stimulating myoblast
				antagonists of the invention)	proliferation, and inhibiting
				include, for example, assays	myoblast proliferation.
				disclosed in: Soeta, C., et al.	
				"Possible role for the c-ski	
				gene in the proliferation of	
				myogenic cells in regenerating	
				skeletal muscles of rats" Dev	
				Growth Differ Apr;43(2):155-	
				64 (2001); Ewton DZ, et al.,	
				"IGF binding proteins-4, -5	
				and -6 may play specialized	
				roles during L6 myoblast	
				proliferation and	
				differentiation" J Endocrinol	

				Mar;144(3):539-53 (1995); and, Pampusch MS, et al., "Effect of transforming growth factor beta on proliferation of L6 and embryonic porcine myogenic cells." J Cell Physiol Jun;143(3):524-8 (1990); the contents of each of which are herein incorporated by reference in their entirety.	
				assays include the rat myoblast L6 cell line. Rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation media.	
112	HDPGI49	1060	Activation of Endothelial Cell p38 or JNK Signaling Pathway.	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred

antibodies and agonists or	embodiment of the invention
antagonists of the invention) to	includes a method for
promote or inhibit cell	stimulating endothelial cell
 proliferation, activation, and	proliferation. An alternative
apoptosis. Exemplary assays	highly preferred embodiment
for JNK and p38 kinase	of the invention includes a
activity that may be used or	method for inhibiting
routinely modified to test JNK	endothelial cell proliferation.
 and p38 kinase-induced	A highly preferred
activity of polypeptides of the	embodiment of the invention
invention (including antibodies	includes a method for
and agonists or antagonists of	stimulating apoptosis of
the invention) include the	endothelial cells. An
assays disclosed in Forrer et	alternative highly preferred
al., Biol Chem 379(8-9):1101-	embodiment of the invention
1110 (1998); Gupta et al., Exp	includes a method for
Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
Soc Symp 64:29-48 (1999);	A highly preferred
Chang and Karin, Nature	embodiment of the invention
 410(6824):37-40 (2001); and	includes a method for
Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
the contents of each of which	alternative highly preferred
 are herein incorporated by	embodiment of the invention
reference in its entirety.	includes a method for
Endothelial cells that may be	inhibiting (e.g., decreasing) the
used according to these assays	activation of and/or
 are publicly available (e.g.,	inactivating endothelial cells.
through the ATCC).	A highly preferred
Exemplary endothelial cells	embodiment of the invention

includes a method for stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic
that may be used according to these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line	venous blood vessels, and are	involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.														~						
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hemodynamic overload, and/or as described below under "Cardiovascular Disorders").	Highly preferred indications include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,
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hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,
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and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include
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					blood disorders (e.g., as
					described below under
					"Immune Activity", "Blood-
					Related Disorders", and/or
					"Cardiovascular Disorders").
					Preferred indications include
					autoimmune diseases (e.g.,
					rheumatoid arthritis, systemic
					lupus erythematosis, multiple
					sclerosis and/or as described
					below) and
					immunodeficiencies (e.g., as
					described below). Additional
					preferred indications include
					inflammation and
					inflammatory disorders (such
					as acute and chronic
					inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
	HDPGP94	1061	Production of	MIP-1alpha FMAT. Assays	A highly preferred
113			MIP1alpha	for immunomodulatory	embodiment of the invention
				proteins produced by activated	includes a method for
				dendritic cells that upregulate	stimulating MIP1a production.
				monocyte/macrophage and T	An alternative highly preferred
				cell chemotaxis are well	embodiment of the invention
				known in the art and may be	includes a method for
				used or routinely modified to	uci
				assess the ability of	MIP1a production. A highly
				polypeptides of the invention	preferred indication is

	(including antibodies and	infection (e.g., an infectious
	agonists or antagonists of the	disease as described below
	invention) to mediate	under "Infectious Disease").
	immunomodulation, modulate	Preferred indications include
	chemotaxis, and modulate T	blood disorders (e.g., as
	cell differentiation. Exemplary	described below under
	assays that test for	"Immune Activity", "Blood-
	immunomodulatory proteins	Related Disorders", and/or
	evaluate the production of	"Cardiovascular Disorders").
	chemokines, such as	Highly preferred indications
 	macrophage inflammatory	include autoimmune diseases
	protein 1 alpha (MIP-1a), and	(e.g., rheumatoid arthritis,
	the activation of	systemic lupus erythematosis,
 	monocytes/macrophages and T	multiple sclerosis and/or as
 	cells. Such assays that may be	described below) and
	used or routinely modified to	immunodeficiencies (e.g., as
	test immunomodulatory and	described below). Additional
 	chemotaxis activity of	highly preferred indications
 	polypeptides of the invention	include inflammation and
	(including antibodies and	inflammatory disorders.
	agonists or antagonists of the	Preferred indications also
	invention) include assays	include anemia, pancytopenia,
	disclosed in Miraglia et al., J	leukopenia, thrombocytopenia,
	Biomolecular Screening 4:193-	Hodgkin's disease, acute
	204(1999); Rowland et al.,	lymphocytic anemia (ALL),
	"Lymphocytes: a practical	plasmacytomas, multiple
	approach" Chapter 6:138-160	myeloma, Burkitt's lymphoma,
	(2000); Satthaporn and	arthritis, AIDS, granulomatous
 	Eremin, J R Coll Surg Ednb	disease, inflammatory bowel
	45(1):9-19 (2001); Drakes et	disease, sepsis, neutropenia,
	al., Transp Immunol 8(1):17-	neutrophilia, psoriasis,

				29 (2000); Verhasselt et al., J	suppression of immune
				Immunol 158:2919-2925	reactions to transplanted
				(1997); and Nardelli et al., J	organs and tissues, hemophilia,
				Leukoc Biol 65:822-828	hypercoagulation, diabetes
				(1999), the contents of each of	mellitus, endocarditis,
				which are herein incorporated	meningitis, Lyme Disease,
				by reference in its entirety.	asthma, and allergy.
				Human dendritic cells that may	Preferred indications also
				be used according to these	include neoplastic diseases
				assays may be isolated using	(e.g., leukemia, lymphoma,
				techniques disclosed herein or	and/or as described below
				otherwise known in the art.	under "Hyperproliferative
				Human dendritic cells are	Disorders"). Highly preferred
				antigen presenting cells in	indications include neoplasms
		,		suspension culture, which,	and cancers, such as, leukemia,
				when activated by antigen	lymphoma, prostate, breast,
				and/or cytokines, initiate and	lung, colon, pancreatic,
				upregulate T cell proliferation	esophageal, stomach, brain,
				and functional activities.	liver, and urinary cancer. Other
					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
	HDPGP94	1061	Production of TNF	TNFa FMAT. Assays for	A highly preferred
113	-		alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for
				macrophages, T cells,	inhibiting (e.g., decreasing)
				fibroblasts, smooth muscle,	TNF alpha production. An
				and other cell types that exert a	alternative highly preferred

				wide variety of inflammatory	embodiment of the invention
				and cytotoxic effects on a	includes a method for
				variety of cells are well known	stimulating (e.g., increasing)
		-		in the art and may be used or	TNF alpha production.
		-	1	routinely modified to assess	Highly preferred indications
				the ability of polypeptides of	include blood disorders (e.g.,
			<del></del>	the invention (including	as described below under
				antibodies and agonists or	"Immune Activity", "Blood-
			-	antagonists of the invention) to	Related Disorders", and/or
				mediate immunomodulation,	"Cardiovascular Disorders"),
				modulate inflammation and	Highly preferred indications
				cytotoxicity. Exemplary	include autoimmune diseases
				assays that test for	(e.g., rheumatoid arthritis,
				immunomodulatory proteins	systemic lupus erythematosis,
				evaluate the production of	Crohn"s disease, multiple
				cytokines such as tumor	sclerosis and/or as described
	•		-1	necrosis factor alpha (TNFa),	below), immunodeficiencies
Ť.				and the induction or inhibition	(e.g., as described below),
				of an inflammatory or	boosting a T cell-mediated
				cytotoxic response. Such	immune response, and
				assays that may be used or	suppressing a T cell-mediated
				routinely modified to test	immune response. Additional
	-		· <b>-</b>	immunomodulatory activity of	highly preferred indications
				polypeptides of the invention	include inflammation and
				(including antibodies and	inflammatory disorders, and
	-			agonists or antagonists of the	treating joint damage in
				invention) include assays	patients with rheumatoid
				disclosed in Miraglia et al., J	arthritis. An additional highly
				Biomolecular Screening 4:193-	preferred indication is sepsis.
		- <del></del> -		204(1999); Rowland et al.,	Highly preferred indications
				"Lymphocytes: a practical	include neoplastic diseases

	paramond! Chanter 6.138 160 La a laybamia lymnhama	(e.g., reukenna, 19mpnoma, (2000); Verhasselt et al., Eur J and/or as described below			Immunol 160(7):3585-3593   highly preferred indications		Immunol 158:2919-2925 cancers, such as, leukemia,	., J		(1999), the contents of each of tumors, and prostate, breast,	which are herein incorporated   lung, colon, pancreatic,	by reference in its entirety.	Human dendritic cells that may   liver and urinary cancer. Other	be used according to these preferred indications include	assays may be isolated using benign dysproliferative	techniques disclosed herein or disorders and pre-neoplastic		Human dendritic cells are example, hyperplasia,	antigen presenting cells in metaplasia, and/or dysplasia.		when activated by antigen an anomia, pancytopenia,	and/or cytokines, initiate and leukopenia, thrombocytopenia,	upregulate T cell proliferation   Hodgkin's disease, acute	and functional activities.   lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,
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					reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
114	HDPHI51	1062	Regulation of transcription through the FAS promoter element in hepatocytes	Assays for the regulation of transcription through the FAS promoter element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the FAS promoter element in a reporter construct and to regulate transcription of FAS, a key enzyme for lipogenesis. FAS promoter is regulated by many transcription factors including SREBP. Insulin increases FAS gene transcription in livers of diabetic mice. This	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel

				assays include rat liver	weight gain. Aditional
	~ <u></u>			hepatoma cell line(s) inducible	highly preferred indications are
				with glucocorticoids, insulin,	complications associated with
				or cAMP derivatives.	insulin resistance.
	HDPHI51	1062	Activation of	Assays for the activation of	A highly preferred
114			transcription	transcription through the	indication is allergy.
			through STAT6	Signal Transducers and	Another highly preferred
			response element in	Activators of Transcription	indication is asthma.
			immune cells (such	(STAT6) response element are	Additional highly preferred
			as T-cells).	well-known in the art and may	indications include
				be used or routinely modified	inflammation and
				to assess the ability of	inflammatory disorders.
				polypeptides of the invention	Preferred indications include
				(including antibodies and	blood disorders (e.g., as
				agonists or antagonists of the	described below under
<del></del>				invention) to regulate STAT6	"Immune Activity", "Blood-
				transcription factors and	Related Disorders", and/or
				modulate the expression of	"Cardiovascular Disorders").
				multiple genes. Exemplary	Preferred indications include
-				assays for transcription	autoimmune diseases (e.g.,
				through the STAT6 response	rheumatoid arthritis, systemic
				element that may be used or	lupus erythematosis, multiple
				routinely modified to test	sclerosis and/or as described
				STAT6 response element	below) and
				activity of the polypeptides of	immunodeficiencies (e.g., as
				the invention (including	described below).
				antibodies and agonists or	Preferred indications include
				antagonists of the invention)	neoplastic diseases (e.g.,
				include assays disclosed in	leukemia, lymphoma,
				Berger et al., Gene 66:1-10	melanoma, and/or as described
				(1998); Cullen and Malm,	below under

"Hyperproliferative Disorders"). Preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, and Lyme Disease.
Methods in Enzymol 216:362-368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); Georas	et al., Blood 92(12):4529-4538	(1998); Moffatt et al.,	Transplantation 69(7):1521-	1523 (2000); Curiel et al., Eur	J Immunol 27(8):1982-1987	(1997); and Masuda et al., J	Biol Chem 275(38):29331-	29337 (2000), the contents of	each of which are herein	incorporated by reference in its	entirety. T cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the SUPT cell line,	which is a suspension culture	of IL-2 and IL-4 responsive T	cells.							
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					An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
115	HDPJF37	1063	Activation of transcription	Assays for the activation of transcription through the	Highly preferred indications include blood disorders (e.g.,
		,	through NFAT response in immune cells (such as T-	Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and	as described below under "Immune Activity", "Blood- Related Disorders", and/or
			cells).	may be used or routinely	"Cardiovascular Disorders").
				of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
				and agonists or antagonists of	systemic lupus erythematosis,
				NFAT transcription factors and	described below),
				modulate expression of genes	immunodeficiencies (e.g., as
				involved in	described below), boosting a T
				Exemplary assays for	response, and suppressing a T
				transcription through the	cell-mediated immune
	-			NFAT response element that	response. Additional highly
				may be used or routinely	preferred indications include
				modified to test NFAT-	inflammation and
		,		response element activity of	inflammatory disorders. An
				polypeptides of the invention	additional highly preferred
				(including antibodies and	indication is infection (e.g., an
				agonists or antagonists of the	infectious disease as described
				invention) include assays	below under "Infectious
				disclosed in Berger et al., Gene	Disease"). Preferred

					organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
116	HDPMM88	1064	Myoblast cell proliferation	Assays for muscle cell proliferation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit myoblast cell proliferation. Exemplary assays for myoblast cell proliferation that may be used or routinely modified to test activity of polypeptides and antibodies of the invention (including agonists or antagonists of the invention) include, for example, assays disclosed in: Soeta, C., et al. "Possible role for the c-ski gene in the proliferation of myogenic cells in regenerating skeletal muscles of rats" Dev Growth Differ Apr;43(2):155-64 (2001); Ewton DZ, et al., "IGF binding proteins-4, -5	Highly preferred indications include diabetes, myopathy, muscle cell atrophy, cancers of muscle (such as, rhabdomyoma, and rhabdosarcoma), cardiovascular disorders (such as congestive heart failure, cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart valve disease, vascular disease, and also as described below under "Cardiovascular Disorders"), stimulating myoblast proliferation.

and -6 may play specialized roles during L6 myoblast proliferation and differentiation." J Endocrinol Mar;144(3):539-53 (1995); and, Pampusch MS, et al., "Effect of transforming growth factor beta on proliferation of L6 and embryonic porcine myogenic cells." J Cell Physiol Jun;143(3):524-8 (1990); the contents of each of which are herein incorporated by reference in their entirety. Exemplary myoblast cells that may be used according to these assays include the rat myoblast L6 cell line. Rat myoblast L6 cells are an adherent rat myoblast cell sare an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation media.	This reporter assay measures activation or inhibition of the NFkB signaling pathway in Ku812 human basophil cell line. Assays for the activation
	Activation or inhibition of transcription through NFKB response element in
	1064
	HDPMM88
	116

or inhibition of transcription	through the NFKB response	element are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate NFKB transcription	factors and modulate	expression of	immunomodulatory genes.	NFkB is important in the	pathogenesis of asthma.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Marone
immune cells (such	as basophils).																													

et al, Int Arch Allergy Immunol 114(3):207-17	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Cells were pretreated with SID	supernatants or controls for 15-	18 hours, and then 10 ng/mL	of TNF was added to stimulate	the NFkB reporter. SEAP	activity was measured after 48	hours. Basophils that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary human basophil	cell lines that may be used	according to these assays	include Ku812, originally	established from a patient with	chronic myelogenous	leukemia. It is an immature	prebasophilic cell line that can	be induced to differentiate into	mature basophils. See, Kishi et	al., Leuk Res. 9:381-390	(1985); Blom et al., Eur J	Immunol. 22:2025-32 (1992),	where the contents of each are	herein incorporated by	reference in its entirety.
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	HDPNC61	1065	Activation of	Assays for the activation of	A highly preferred indication
117			transcription	transcription through the	is obesity and/or complications
	,		through cAMP	cAMP response element are	associated with obesity.
			response element	well-known in the art and may	Additional highly preferred
	·		(CRE) in pre-	be used or routinely modified	indications include weight loss
			adipocytes.	to assess the ability of	or alternatively, weight gain.
				polypeptides of the invention	An additional highly preferred
				(including antibodies and	indication is diabetes mellitus.
				agonists or antagonists of the	An additional highly preferred
				invention) to increase cAMP,	indication is a complication
				regulate CREB transcription	associated with diabetes (e.g.,
				factors, and modulate	diabetic retinopathy, diabetic
				expression of genes involved	nephropathy, kidney disease
				in a wide variety of cell	(e.g., renal failure,
				functions. For example, a	nephropathy and/or other
				3T3-L1/CRE reporter assay	diseases and disorders as
				may be used to identify factors	described in the "Renal
				that activate the cAMP	Disorders" section below),
				signaling pathway. CREB	diabetic neuropathy, nerve
				plays a major role in	disease and nerve damage
				adipogenesis, and is involved	(e.g., due to diabetic
				in differentiation into	neuropathy), blood vessel
				adipocytes. CRE contains the	blockage, heart disease, stroke,
				binding sequence for the	impotence (e.g., due to diabetic
				transcription factor CREB	neuropathy or blood vessel
				(CRE binding protein).	blockage), seizures, mental
				Exemplary assays for	confusion, drowsiness,
				transcription through the	nonketotic hyperglycemic-
				cAMP response element that	hyperosmolar coma,
				may be used or routinely	cardiovascular disease (e.g.,
				modified to test cAMP-	heart disease, atherosclerosis,

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	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	Additional highly preferred	indications are complications	associated with insulin	resistance.							
	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Reusch	et al., Mol Cell Biol	20(3):1008-1020 (2000); and	Klemm et al., J Biol Chem	273:917-923 (1998), the	contents of each of which are	herein incorporated by	reference in its entirety. Pre-	adipocytes that may be used	according to these assays are	publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	
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				through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	
117	HDPNC61	1065	Activation of transcription through GAS response element in immune cells (such as eosinophils).	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate gene expression (commonly via STAT transcription factors) involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene	Highly preferred indications include asthma, allergy, hypersensitivity reactions, inflammation, and inflammatory disorders. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Blood-Related Disorders"), autoimmune Activity", and "upus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting an eosinophil-mediated immune response and, alternatively, suppressing an eosinophil-mediated immune response.

Malm, Methods in Enzymol 216:362-368 (1992); Henthorn	85:6342-6346 (1988);	Matikainen et al., Blood	Henttinen et al., J Immunol	155(10):4582-4587 (1995); the	contents of each of which are	herein incorporated by	reference in its entirety.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to activate or	inhibit activation of immune	cells include assays disclosed	and/or cited in: Mayumi M.,	"EoL-1, a human eosinophilic	cell line" Leuk Lymphoma;	Jun;7(3):243-50 (1992);	Bhattacharya S, "Granulocyte	macrophage colony-	stimulating factor and	interleukin-5 activate STAT5	and induce CIS1 mRNA in	human peripheral blood	eosinophils" Am J Respir Cell
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	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell	growth. An alternative highly
Mol Biol; Mar;24(3):312-6 (2001); and, Du J, et al., "Engagement of the CrkL adapter in interleukin-5 signaling in eosinophils" J Biol Chem; Oct 20;275(42):33167-75 (2000); the contents of each of which are herein incorporated by reference in its entirety. Exemplary cells that may be used according to these assays include eosinophils. Eosinophils are a type of immune cell important in the late stage of allergic reactions; they are recruited to tissues and mediate the inflammtory response of late stage allergic reaction. Increases in GAS mediated transcription in eosinophils is typically a result of STAT activation, normally a direct consequence of interleukin or other cytokine receptor stimulation (e.g. IL3, IL5 or GMCSF).	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell	proliferation or differentiation
•	Activation of Endothelial Cell ERK Signaling Pathway	, univery.
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f the	poq	l cell	ferred	ntion		ell	tive	ment	sa		tion.		ntion				red	ntion		ng)	cells.		ntion		sing)	n. An	red	ntion		of
preferred embodiment of the	invention includes a method	for inhibiting endothelial cell	growth. A highly preferred	embodiment of the invention	includes a method for	stimulating endothelial cell	proliferation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting	endothelial cell proliferation.	referred	embodiment of the invention	includes a method for	stimulating apoptosis of	l cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	referred	embodiment of the invention	includes a method for	stimulating (e.g., increasing)	endothelial cell activation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting the activation of
preferred e	invention i	for inhibiti	growth.	embodime	includes a	stimulating	proliferation	highly pred	of the inve	method for	endothelia	A highly preferred	embodime	includes a	stimulating	endothelial cells. An	alternative	embodime	includes a	inhibiting	apoptosis (	A highly preferred	embodime	includes a	stimulating	endothelia	alternative	embodime	includes a	inhibiting
					nists of			tiation.	ERK					tibodies			rer et					Res	; Chang		l); and	ys Mol	(1999);	which	l by	,
wn in the	l or routine	assess the	des of the	ncluding at	s or antago	n) to prom	proliferation	and differer	assays for l	ity that ma	inely modi	nase-induc	olypeptide	ncluding an	s or antago	n) include	osed in For	em 379(8-9	); Berra et	narmacol	1178 (200	, Exp Cell	504 (1999)	Vature	37-40 (200	Prog Bioph	):479-500 (	of each of	ncorporated	its entirety
are well known in the art and	may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to promote or	inhibit cell proliferation,	activation, and differentiation.	Exemplary assays for ERK	kinase activity that may be	used or routinely modified to	test ERK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Berra et al.,	Biochem Pharmacol	60(8):1171-1178 (2000);	Gupta et al., Exp Cell Res	247(2):495-504 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.
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	(e.g., decreasing) and/or	inactivating endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating endothelial cell	differentiation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting	endothelial cell differentiation.	A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis.	A highly preferred	embodiment of the invention	includes a method for reducing	cardiac hypertrophy. An	alternative highly preferred	embodiment of the invention	includes a method for inducing	cardiac hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative
	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line	venous blood vessels, and are	involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.													-		
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Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or
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Eardiovascularization. Highly preferred indications include antiangiogenic activity to treat solid tumors.	leukemias, and Kaposi"s sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer,	such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis,	hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangioma,	lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and	urinary cancer. Freferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease,

				such as, atherosclerosis.
				harate thought acceptant of the control of the cont
				nypertension, coronary artery
				disease, inflammatory
			-	vasculitides, Reynaud's
				disease and Reynaud"s
				phenomenom, aneurysms,
				restenosis; venous and
			-	lymphatic disorders such as
	,			thrombophlebitis,
-				lymphangitis, and
			-	lymphedema; and other
				vascular disorders such as
			-	peripheral vascular disease,
				and cancer. Highly
•				preferred indications also
				include trauma such as
				wounds, burns, and injured
				tissue (e.g., vascular injury
				such as, injury resulting from
				balloon angioplasty, and
				atheroschlerotic lesions),
	-		4	implant fixation, scarring,
				ischemia reperfusion injury,
	-			rheumatoid arthritis,
				cerebrovascular disease, renal
				diseases such as acute renal
	,			failure, and osteoporosis.
				Additional highly preferred
				indications include stroke,
				graft rejection, diabetic or
		į		other retinopathies, thrombotic

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	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity"; "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	preferred indications include	inflammation and	inflammatory disorders (such	as acute and chronic	inflammatory diseases, e.g.,
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vel disease se), and pain	d indications diseases mphoma, de below iferative ly preferred e neoplasms as, for a, lymphoma noma, noma, noma, no, pancreatic, ach, brain, cancer. Other ons include rative -neoplastic as, for asia, or dysplasia. ons include ases (e.g., tis, systemic sis, multiple s described
inflammatory bowel disease and Crohn's disease), and pain management.	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, non-Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described
	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol
	(such in it is in it
	Activation of transcription through GAS response elem immune cells as T-cells).
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et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety.  Exemplary human T cells, such as the MOLT4 cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).	<u> </u>			ya), the   immune response. Additional that are   preferred indications include	inflammation and			l line,   include blood disorders (e.g.,		-	-		and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an	infectious disease as described	below under "Infectious	(Disease"). An additional	preferred indication is	idiopathic pulmonary fibrosis.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	acute lymphocytic anemia	(ALL), plasmacytomas,
	et al., Proc Natl Acad S 85:6342-6346 (1988);	Matikainen et al., Blooc   93(6):1980-1991 (1999)	Henttinen et al., J Immu	155(10):4582-4587 (19)   contents of each of whi	herein incorporated by	reference in its entirety.	Exemplary human T cel	such as the MOLT4 cell	that may be used accord	these assays are publicly	available (e.g., through	ATCC).																

and the induction of	chemotactic responses in	immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Cocchi et al., Science	270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp	Immunol 101(3):398-407	(1995), the contents of each of	which are herein incorporated	by reference in its entirety.	Epithelial cells were isolated	from bronchia/trachea	immediately postmortem from	humans who were free of	known respiratory diseases.	See Wu et al., Am Rev Respir	Dis. 132(2):311-20 (1985), the	contents of which are herein	incorporated by reference in its
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				entirety.	
	HDPND46	1066	Activation of	Kinase assay. Kinase assays,	A highly preferred
118			Adipocyte PI3	for example an GSK-3 assays,	embodiment of the invention
			Kinase Signalling	for PI3 kinase signal	includes a method for
			Pathway	transduction that regulate	increasing adipocyte survival
				glucose metabolism and cell	An alternative highly preferred
				survival are well-known in the	embodiment of the invention
				art and may be used or	includes a method for
				routinely modified to assess	decreasing adipocyte survival.
		,		the ability of polypeptides of	A preferred embodiment of the
				the invention (including	invention includes a method
				antibodies and agonists or	for stimulating adipocyte
				antagonists of the invention) to	proliferation. An alternative
				promote or inhibit glucose	highly preferred embodiment
				metabolism and cell survival.	of the invention includes a
				Exemplary assays for PI3	method for inhibiting
				kinase activity that may be	adipocyte proliferation. A
				used or routinely modified to	preferred embodiment of the
				test PI3 kinase-induced activity	invention includes a method
				of polypeptides of the	for stimulating adipocyte
				invention (including antibodies	differentiation. An alternative
				and agonists or antagonists of	highly preferred embodiment
				the invention) include assays	of the invention includes a
				disclosed in Forrer et al., Biol	method for inhibiting
				Chem 379(8-9):1101-1110	adipocyte differentiation.
				(1998); Nikoulina et al.,	Highly preferred indications
-1				Diabetes 49(2):263-271	include endocrine disorders
				(2000); and Schreyer et al.,	(e.g., as described below under
				Diabetes 48(8):1662-1666	"Endocrine Disorders").
				(1999), the contents of each of	Preferred indications include
				which are herein incorporated	neoplastic diseases (e.g.,

	by reference in its entirety.	lipomas, liposarcomas, and/or
	Mouse adipocyte cells that	as described below under
	may be used according to these	"Hyperproliferative
	assays are publicly available	Disorders"), blood disorders
 	(e.g., through the ATCC).	(e.g., hypertension, congestive
	Exemplary mouse adipocyte	heart failure, blood vessel
 	cells that may be used	blockage, heart disease, stroke,
	according to these assays	impotence and/or as described
	include 3T3-L1 cells. 3T3-L1	below under "Immune
•	is an adherent mouse	Activity", "Cardiovascular
 -	preadipocyte cell line that is a	Disorders", and/or "Blood-
-	continous substrain of 3T3	Related Disorders"), immune
 	fibroblast cells developed	disorders (e.g., as described
	through clonal isolation and	below under "Immune
	undergo a pre-adipocyte to	Activity"), neural disorders
	adipose-like conversion under	(e.g., as described below under
-	appropriate differentiation	"Neural Activity and
	conditions known in the art.	Neurological Diseases"), and
		infection (e.g., as described
-		below under "Infectious
 		Disease"). A highly
		preferred indication is diabetes
		mellitus. An additional
		highly preferred indication is a
		complication associated with
		diabetes (e.g., diabetic
		retinopathy, diabetic
		nephropathy, kidney disease
		(e.g., renal failure,
		nephropathy and/or other
		diseases and disorders as

below, especially of the urinary tract and skin), carpal tunnel syndrome and	Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly	preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with	insulin resistance. Additional highly preferred indications are disorders of the	musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein.  Additional highly preferred	indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia,	and kidney diseases or disorders. Highly preferred indications include neoplasms and cancer, such as, lipoma,
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					liposarcoma, lymphoma, leukemia and breast, colon, and kidney cancer. Additional highly preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
118	HDPND46	1066	Production of IL-4	IL-4 FMAT. Assays for immunomodulatory proteins secreted by TH2 cells that stimulate B cells, T cells, macrophages and mast cells and promote polarization of CD4+ cells into TH2 cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, stimulate immune cells, modulate immune cells, modulate	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-4 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-4 production. A highly preferred indication includes asthma. A highly preferred indication includes allergy. A highly preferred indication includes indication includes rhinitis. Additional highly preferred indication and

teins of and and me cells, sells. sells. sells. sells. sells. of the ssays al., J d.4:193- al., J d.1194); ol Bagley S:257- Craaff xxford) he	of d d d d d d d d d d d d d d d d d d d	of of a d d d d d d d d d d d d d d d d d d
cell-mediated immunity.  Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-4, and the stimulation of immune cells, such as B cells, T cells, macrophages and mast cells.  Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):277-283 (1194); Yssel et al., Res Immunol 1(3):257-261 (2000); and van der Graaff et al., Rheumatology (Oxford) 38(3):214-220 (1999), the contents of each of which are herein incorporated by	Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-4, and the stimulation of immune cells, such as B cells, T cells, macrophages and mast cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):277-283 (1194); Yssel et al., Nat Immunol 1(3):257-261 (2000); and van der Graaff et al., Rheumatology (Oxford) 38(3):214-220 (1999), the contents of each of which are herein incorporated by	cell-mediated immunity.  Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-4, and the stimulation of immune cells, such as B cells, T cells, macrophages and mast cells.  Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):277-283 (1194); Yssel et al., Res Immunol 144(8):610-616 (1993); Bagley et al., Nat Immunol 1(3):257-261 (2000); and van der Graaff et al., Rheumatology (Oxford) 38(3):214-220 (1999), the contents of each of which are herein incorporated by

				Human T cells that may be	below) and
			-	used according to these assays	immunodeficiencies (e.g., as
				may be isolated using	described below). Preferred
				techniques disclosed herein or	indications include anemia,
				otherwise known in the art.	pancytopenia, leukopenia,
				Human T cells are primary	thrombocytopenia, Hodgkin's
				human lymphocytes that	disease, acute lymphocytic
				mature in the thymus and	anemia (ALL),
				express a T cell receptor and	plasmacytomas, multiple
				CD3, CD4, or CD8. These	myeloma, Burkitt's lymphoma,
				cells mediate humoral or cell-	arthritis, AIDS, granulomatous
				mediated immunity and may	disease, inflammatory bowel
				be preactivated to enhance	disease, sepsis, neutropenia,
				responsiveness to	neutrophilia, psoriasis,
				immunomodulatory factors.	suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
			-		below under "Infectious
					Disease").
	HDPND46	1066	Production of IL-8	Assays measuring production	Highly preferred indications
118			by by endothelial	of IL-8 are well known in the	include immunological and
			cells (such as	art and may be used or	inflammatory disorders (e.g.,
			Human Umbilical	routinely modified to assess	such as allergy, asthma,
			Cord Endothelial	the ability of polypeptides of	leukemia, etc. and as described
			Cells).	the invention (including	below under "Immune

_		antihodies and agonists or	Activity" and "Blood-Related
 		anticodics and agoinsts of	Discussion of the Constitution of the Constitu
 		antagonists of the invention) to	Disoraers ). Hignly preferred
 		regulate production and/or	indications also includie
 		secretion of IL-8. For	autoimmune disorders (e.g.,
		example, FMAT may be used	rheumatoid arthritis, systemic
 		or routinely modified to assess	lupus erythematosis, Crohn"s
 		the ability of polypeptides of	disease, multiple sclerosis
		the invention (including	and/or as described below),
		antibodies and agonists or	neoplastic disorders (e.g.,
		antagonists of the invention) to	organ cancers such as lung,
 		regulate production and/or	liver, colon cancer, and/or as
 		secretion of IL-8 from	described below under
 		endothelial cells (such as	"Hyperproliferative
 		human umbilical vein	Disorders"), and
 		endothelial cells (HUVEC)).	cardiovascular disorders (e.g.
 		HUVECs are endothelial cells	such as described below under
		which line venous blood	"Cardiovascular Disorders").
		vessels, and are involved in	Preferred indications include
		functions that include, but are	thrombosis, bacteremia and
 		not limited to, angiogenesis,	sepsis syndrome and
 		vascular permeability, vascular	consequent complications
 		tone, and immune cell	(such as acute respiratory
		extravasation. Endothelial	distress syndrome and
 		cells play a pivotal role in the	systemic ischemia-reperfusion
 		initiation and perpetuation of	resulting from septic shock),
 		inflammation and secretion of	restnosis and atherosclerosis.
		IL-8 may play an important	
 		role in recruitment and	
 		activation of immune cells	
 		such as neutrophils,	
 		macrophages, and	

	neasuring Preferred embodiments of the invention include using	may		-	ention		agonists or antagonists of the   Inflammation, Vascular	invention) to regulate ICAM-1   Disease, Athereosclerosis,		that may be used or routinely	modified to measure ICAM-1	nclude assays	Takacs P, et al,	5(2):279-281		Miyamoto K, et	(2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-	Miyamoto K, et thol, 156(5):1733- , the contents of	Miyamoto K, et thol, 156(5):1733- , the contents of this herein	(2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its	Miyamoto K, et thol, 156(5):1733- , the contents of this herein lby reference in its lls that may be	Miyamoto K, et thol, 156(5):1733- , the contents of this herein lby reference in its lls that may be ung to these assays	(2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g.,	Miyamoto K, et thol, 156(5):1733- , the contents of this herein lay reference in its lls that may be mig to these assays available (e.g.,	Miyamoto K, et thol, 156(5):1733- , the contents of this herein less reference in its lls that may be ing to these assays available (e.g., ATCC) and/or inely generated.	al., Am J Pathol, 156(5):1733- 1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated.  Exemplary cells that may be	Miyamoto K, et thol, 156(5):1733- , the contents of this herein its leverence in its lls that may be mg to these assays available (e.g., ATCC) and/or inely generated.	al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular
lymphocytes.	Assays for measuring expression of ICAM-1 are	rell-known in the	e used or routine	to assess the ability of	olypeptides of th	(including antibodies and	gonists or antago	rvention) to regu	xpression. Exen	nat may be used	nodified to meas	expression include assays	disclosed in: Takacs P, et al,	ASEB J, 15(2):2		2001); and, Miya	2001); and, Miya l., Am J Pathol,	(2001); and, Miyamoto K, et al., Am J Pathol, 156(5):173: 1739 (2000), the contents of	(2001); and, Miyamoto al., Am J Pathol, 156(5) 1739 (2000), the conter each of which is herein	2001); and, Miya I., Am J Pathol, 739 (2000), the of ach of which is I	(2001); and, Miyamoto K, eal., Am J Pathol, 156(5):171739 (2000), the contents of each of which is herein incorporated by reference in entirety. Cells that may be	2001); and, Miye I., Am J Pathol, 739 (2000), the ach of which is Incorporated by rutirety. Cells the sed according to	(2001); and, Miyamoto K, al., Am J Pathol, 156(5):17.1739 (2000), the contents of each of which is herein incorporated by reference in entirety. Cells that may be used according to these assare publicly available (e.g.,	(2001); and, Miyamoto K, al., Am J Pathol, 156(5):17 1739 (2000), the contents each of which is herein incorporated by reference i entirety. Cells that may be used according to these ass are publicly available (e.g., through the ATCC) and/or	(2001); and, Miyamoto K, e al., Am J Pathol, 156(5):173 1739 (2000), the contents of each of which is herein incorporated by reference in entirety. Cells that may be used according to these assa are publicly available (e.g., through the ATCC) and/or may be routinely generated.	2001); and, Miye I., Am J Pathol, 739 (2000), the ach of which is I neorporated by rentirety. Cells the sed according to re publicly avail arough the ATC hay be routinely exemplary cells the exemplants.	2001); and, Miye I., Am J Pathol, 739 (2000), the ach of which is 1 corporated by 1 rutirety. Cells this sed according to re publicly avail arough the ATC aay be routinely exemplary cells to sed according to sed according to	(2001); and, Miyamot al., Am J Pathol, 156( 1739 (2000), the conte each of which is herein incorporated by refere entirety. Cells that ma used according to thes are publicly available through the ATCC) an may be routinely gene Exemplary cells that n used according to thes include microvascular
	Jo uo		<u>.</u>	<u> </u>	<u></u>	<u>~</u>	8			+7	<u> </u>		<u> </u>					) 8 1				<u> </u>						
	Producti ICAM-1		<del>-</del>																									
	1067																											
	HDPOE32																											
	119	\ \ \ -													_													

120			ICAM-1	expression of ICAM-1 are	invention include using
				well-known in the art and may	polypeptides of the invention
				be used or routinely modified	(or antibodies, agonists, or
				to assess the ability of	antagonists thereof) in
				polypeptides of the invention	detection, diagnosis,
				(including antibodies and	prevention, and/or treatment of
				agonists or antagonists of the	Inflammation, Vascular
				invention) to regulate ICAM-1	Disease, Athereosclerosis,
				expression. Exemplary assays	Restenosis, and Stroke
				that may be used or routinely	
				modified to measure ICAM-1	
				expression include assays	
				disclosed in: Takacs P, et al,	
				FASEB J, 15(2):279-281	
				(2001); and, Miyamoto K, et	
				al., Am J Pathol, 156(5):1733-	
				1739 (2000), the contents of	
				each of which is herein	
				incorporated by reference in its	
				entirety. Cells that may be	
				used according to these assays	
				are publicly available (e.g.,	
				through the ATCC) and/or	
				may be routinely generated.	
				Exemplary cells that may be	
	,			used according to these assays	
				include microvascular	
				endothelial cells (MVEC).	
	НДРОН06	1068	Production of IL-10	Assays for production of IL-10	Highly preferred indications
120			and activation of T-	and activation of T-cells are	include allergy and asthma.
			cells.	well known in the art and may	Additional highly preferred

indications include immune	and hematopoietic disorders	(e.g., as described below under	"Immune Activity", and	"Blood-Related Disorders"),	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, Crohn"s	disease, multiple sclerosis	and/or as described below),	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune	response, and suppressing a T	cell-mediated immune	response.															
be used or routinely modified	to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to stimulate or	inhibit production of IL-10	and/or activation of T-cells.	Exemplary assays that may be	used or routinely modified to	assess the ability of	polypeptides and antibodies of	the invention (including	agonists or antagonists of the	invention) to modulate IL-10	production and/or T-cell	proliferation include, for	example, assays such as	disclosed and/or cited in:	Robinson, DS, et al., "Th-2	cytokines in allergic disease"	Br Med Bull; 56 (4): 956-968	(2000), and Cohn, et al., "T-	helper type 2 cell-directed	therapy for asthma"	Pharmacology & Therapeutics;	88: 187-196 (2000); the	contents of each of which are	herein incorporated by	reference in their entirety.	Exemplary cells that may be
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			•									_~							- 15-15							·				

ssays nay be Th2 Is are rete IL6. tion or role er 2 vitro sing ral ed	of Preferred embodiments of the invention include using polypeptides of the invention nent (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Cancer, Wound Healing, and bodies Inflamation. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperprofiferative").
used according to these assays include Th2 cells. IL10 secreted from Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression
	transcription transcription through GAS response element in epithelial cells (such as HELA cells).
	HDPOZ56
	121

Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	include inflammation and	inflammatory disorders.	•										.,,				
involved in a wide variety of	cell functions. Exemplary	assays for transcription	through the GAS response	element that may be used or	routinely modified to test	GAS-response element activity	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in: You M, et al, J	Biol Chem, 272(37):23376-	23381(1997); Min W, et al.,	Circ Res, 83(8):815-823	(1998); Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.	Epithelial cells that may be	used according to these assays	are publicly available (e.g.,
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<del></del>	HDPOZ56	1069	Activation of	through the ATCC).  Exemplary epithelial cells that may be used according to these assays include the HELA cell line.  Kinase assay. INK and p38	A highly preferred
			Endothelial Cell	kinase assays for signal	embodiment of the invention
			p38 or JNK. Signaling Pathway.	transduction that regulate cell proliferation, activation, or	includes a method for stimulating endothelial cell
				apoptosis are well known in	growth. An alternative highly
				the art and may be used or	preferred embodiment of the
				routinely modified to assess	invention includes a method
				the ability of polypeptides of	for inhibiting endothelial cell
				the invention (including	growth. A highly preferred
				antibodies and agonists or	embodiment of the invention
		-		antagonists of the invention) to	includes a method for
				promote or inhibit cell	stimulating endothelial cell
				proliferation, activation, and	proliferation. An alternative
				apoptosis. Exemplary assays	highly preferred embodiment
				for JNK and p38 kinase	of the invention includes a
				activity that may be used or	method for inhibiting
				routinely modified to test JNK	endothelial cell proliferation.
				and p38 kinase-induced	A highly preferred
				activity of polypeptides of the	embodiment of the invention
				invention (including antibodies	includes a method for
				and agonists or antagonists of	stimulating apoptosis of
				the invention) include the	endothelial cells. An
				assays disclosed in Forrer et	alternative highly preferred
				al., Biol Chem 379(8-9):1101-	embodiment of the invention
				1110 (1998); Gupta et al., Exp	includes a method for
				Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)

(1999);	(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
Soc Sym	Soc Symp 64:29-48 (1999);	A highly preferred
Chang an	Chang and Karin, Nature	embodiment of the invention
410(682	410(6824):37-40 (2001); and	includes a method for
Cobb MI	Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
Biol 71(	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
the conte	the contents of each of which	alternative highly preferred
are herei	are herein incorporated by	embodiment of the invention
reference	reference in its entirety.	includes a method for
Endothel	Endothelial cells that may be	inhibiting (e.g., decreasing) the
used acc	used according to these assays	activation of and/or
are publi	are publicly available (e.g.,	inactivating endothelial cells.
through	through the ATCC).	A highly preferred
Exempla	Exemplary endothelial cells	embodiment of the invention
that may	that may be used according to	includes a method for
these ass	these assays include human	stimulating angiogenisis. An
umbilica	umbilical vein endothelial cells	alternative highly preferred
(HUVEC	(HUVEC), which are	embodiment of the invention
endothel	endothelial cells which line	includes a method for
venous b	venous blood vessels, and are	inhibiting angiogenesis. A
involved	involved in functions that	highly preferred embodiment
include,	include, but are not limited to,	of the invention includes a
angioger	angiogenesis, vascular	method for reducing cardiac
permeab	permeability, vascular tone,	hypertrophy. An alternative
and imm	and immune cell extravasation.	highly preferred embodiment
		of the invention includes a
		method for inducing cardiac
		hypertrophy. Highly
		preferred indications include
		neoplastic diseases (e.g., as
		described below under

"Hyperproliferative Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that
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also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or
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other retinopathies, thrombotic and coagulative disorders,	vascularitis, lymph angiogenesis, sexual disorders,	age-related macular degeneration, and treatment	/prevention of endometriosis	Additional highly preferred	indications include fibromas,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	preferred indications include	inflammation and	inflammatory disorders (such	as acute and chronic
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inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting apoptosis of embodiment of the invention includes a method for inhibiting apoptosis of endothelial cells. An
	Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention, activation, and apoptosis. Exemplary assays for JNK kinase activity that may be used or routinely modified to test JNK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1999); Kyriakis JM, Biochem Soc. Symp 64-29-48 (1999);
	Activation of Endothelial Cell JNK Signaling Pathway.
	1070
	HDPSP54
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highly preferred embodiment of the invention includes a	method for stimulating	endothelial cell activation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting the activation of	and/or inactivating endothelial	cells. A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention		inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment		method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system
Chang and Karin, Nature 410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line	venous blood vessels, and are	involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.								
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to treat solid tumors, leukemias, and Kaposi"s
Highly preferred indications include neoplasms and cancer, such as, Kaposi's sarcoma,
hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis,
hemangioendothelioma, angiosarcoma, haemangiopericytoma,
lymphangiosarcoma. Highly preferred indications also include cancers such as,
prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred
dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia,
metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis, hypertension, coronary artery

disease, inflammatory vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph
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angiogenesis, sexual disorders,	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	preferred indications include	inflammation and	inflammatory disorders (such	as acute and chronic	inflammatory diseases, e.g.,	inflammatory bowel disease	and Crohn's disease), and pain
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					management.
	HDPSP54	1070	Regulation of	Caspase Apoptosis. Assays	A highly preferred
122			apoptosis in	for caspase apoptosis are well	indication is diabetes mellitus.
			pancreatic beta	known in the art and may be	An additional highly preferred
			cells.	used or routinely modified to	indication is a complication
				assess the ability of	associated with diabetes (e.g.,
				polypeptides of the invention	diabetic retinopathy, diabetic
				(including antibodies and	nephropathy, kidney disease
,				agonists or antagonists of the	(e.g., renal failure,
				invention) to promote caspase	nephropathy and/or other
				protease-mediated apoptosis.	diseases and disorders as
				Apoptosis in pancreatic beta is	described in the "Renal
				associated with induction and	Disorders" section below),
				progression of diabetes.	diabetic neuropathy, nerve
				Exemplary assays for caspase	disease and nerve damage
				apoptosis that may be used or	(e.g., due to diabetic
				routinely modified to test	neuropathy), blood vessel
				capase apoptosis activity of	blockage, heart disease, stroke,
				polypeptides of the invention	impotence (e.g., due to diabetic
				(including antibodies and	neuropathy or blood vessel
				agonists or antagonists of the	blockage), seizures, mental
				invention) include the assays	confusion, drowsiness,
				disclosed in: Loweth, AC, et	nonketotic hyperglycemic-
				al., FEBS Lett, 400(3):285-8	hyperosmolar coma,
				(1997); Saini, KS, et al.,	cardiovascular disease (e.g.,
				Biochem Mol Biol Int,	heart disease, atherosclerosis,
				39(6):1229-36 (1996);	microvascular disease,
				Krautheim, A., et al., Br J	hypertension, stroke, and other
				Pharmacol, 129(4):687-94	diseases and disorders as
				(2000); Chandra J, et al.,	described in the
		and the second s		Diabetes, 50 Suppl 1:S44-7	"Cardiovascular Disorders"

			(2001): Sub K et al I	section below) dyslinidemia
			[mm]mol 166(7):4481-9	endocrine disorders (as
			(2001): Teiedo I et al FFBS	described in the "Endocrine
			Lett, 459(2):238-43 (1999);	Disorders" section below),
			Zhang, S., et al., FEBS Lett,	neuropathy, vision impairment
			455(3):315-20 (1999); Lee et	(e.g., diabetic retinopathy and
		-	al., FEBS Lett 485(2-3): 122-	blindness), ulcers and impaired
			126 (2000); Nor et al., J Vasc	wound healing, and infection
-			Res 37(3): 209-218 (2000);	(e.g., infectious diseases and
	-		and Karsan and Harlan, J	disorders as described in the
			Atheroscler Thromb 3(2): 75-	"Infectious Diseases" section
			80 (1996); the contents of each	below, especially of the
			of which are herein	urinary tract and skin), carpal
			incorporated by reference in its	tunnel syndrome and
			entirety. Pancreatic cells that	Dupuytren's contracture).
			may be used according to these	An additional highly preferred
			assays are publicly available	indication is obesity and/or
			(e.g., through the ATCC)	complications associated with
			and/or may be routinely	obesity. Additional highly
•••			generated. Exemplary	preferred indications include
			pancreatic cells that may be	weight loss or alternatively,
			used according to these assays	weight gain. Aditional
			include RIN-m. RIN-m is a	highly preferred indications are
			rat adherent pancreatic beta	complications associated with
			cell insulinoma cell line	insulin resistance.
			derived from a radiation	
			induced transplantable rat islet	
			cell tumor. The cells produce	
			and secrete islet polypeptide	
			hormones, and produce insulin,	
			somatostatin, and possibly	

	Highly preferred indications include allergy and asthma. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response.
glucagon. ATTC: #CRL-2057 Chick et al. Proc. Natl. Acad. Sci. 1977 74:628; AF et al. Proc. Natl. Acad. Sci. 1980 77:3519.	Assays for production of IL-10 and activation of T-cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit production of IL-10 and/or activation of T-cells. Exemplary assays that may be used or routinely modified to assess the ability of polypeptides and antibodies of the invention (including agonists or antagonists of the invention) to modulate IL-10 production and/or T-cell proliferation include, for example, assays such as disclosed and/or cited in: Robinson, DS, et al., "Th-2 cytokines in allergic disease." Br Med Bull; 56 (4): 956-968 (2000), and Cohn, et al., "T-
	Production of IL-10 and activation of T-cells.
	1070
	HDPSP54
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	A highly preferred embodiment of the invention includes a method for	stimulating the production of IFNg. An alternative highly
helper type 2 cell-directed therapy for asthma" Pharmacology & Therapeutics; 88: 187-196 (2000); the contents of each of which are herein incorporated by reference in their entirety.  Exemplary cells that may be used according to these assays include Th2 cells. IL10 secreted from Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be	a prointlammatory cytokine. IFNg promotes TH1 and
	Production of IFNgamma using a T cells	
	1072	
	HDPTK41	
	124	

preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood	disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"),	and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant	osteoporosis, and/or as described below under "Infectious Disease"). Highly preferred indications include autoimmune disease (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiency (e.g., as described below), boosting a T cell-mediated immune response, and	suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and
inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression.	Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2	helper cell functions are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention	(including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, regulate inflammatory activities, modulate TH2 helper cell function, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of	cytokines, such as Interferon gamma (IFNg), and the activation of T cells. Such assays that may be used or
				*

routinely modified to test inflammatory disorders.	immunomodulatory activity of   Additional preferred	polypeptides of the invention   indications include idiopathic	(including antibodies and pulmonary fibrosis. Highly	the	invention) include the assays neoplastic diseases (e.g.,	disclosed in Miraglia et al., J leukemia, lymphoma,	Biomolecular Screening 4:193-   melanoma, and/or as described	204 (1999); Rowland et al., below under	"Lymphocytes: a practical "Hyperproliferative	approach" Chapter 6:138-160 Disorders"). Highly preferred	(2000); Gonzalez et al., J Clin   indications include neoplasms	Lab Anal 8(5):225-233 (1995); and cancers, such as, for	Billiau et al., Ann NY Acad example, leukemia, lymphoma,	Sci 856:22-32 (1998); Boehm   melanoma, and prostate,	et al., Annu Rev Immunol breast, lung, colon, pancreatic,		Rheumatology (Oxford)   liver and urinary cancer. Other	38(3):214-20 (1999), the preferred indications include	contents of each of which are benign dysproliferative		reference in its entirety.	Human T cells that may be example, hyperplasia,	used according to these assays   metaplasia, and/or dysplasia.	may be isolated using   Preferred indications include	techniques disclosed herein or anemia, pancytopenia,	otherwise known in the art.   leukopenia, thrombocytopenia,	Human T cells are primary Hodgkin's disease, acute	human lymphocytes that   lymphocytic anemia (ALL),	mature in the thymus and plasmacytomas, multiple	oversage of Call moonter and my lamb Durkitt's lymphome
routinely	nonumi	polypepti	(including	agonists	invention	disclosed	Biomolec	204 (199	"Lympho	approach	(2000); G	Lab Anal	Billiau et	Sci 856:2	et al., An	15:749-7	Rheumat	38(3):21	contents	herein inc	reference	Human T	used acco	may be is	technique	otherwise	Human I	human ly	mature in	מ אסגעיינאס

				CD3, CD4, or CD8. These cells mediate humoral or cellmediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and alleroy.
126	HDPUH26	1074	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method

		and agonists or antagonists of	for stimulating (e.g.,
		the invention) include the	increasing) adipocyte
		assays disclosed in Forrer et	activation. An alternative
		al., Biol Chem 379(8-9):1101-	highly preferred embodiment
		1110 (1998); Le Marchand-	of the invention includes a
		Brustel Y, Exp Clin	method for inhibiting the
		Endocrinol Diabetes	activation of (e.g., decreasing)
		107(2):126-132 (1999);	and/or inactivating adipocytes.
		Kyriakis JM, Biochem Soc	Highly preferred indications
		Symp 64:29-48 (1999); Chang	include endocrine disorders
		and Karin, Nature	(e.g., as described below under
		410(6824):37-40 (2001); and	"Endocrine Disorders").
		Cobb MH, Prog Biophys Mol	Highly preferred indications
		Biol 71(3-4):479-500 (1999);	also include neoplastic
		the contents of each of which	diseases (e.g., lipomas,
		are herein incorporated by	liposarcomas, and/or as
		reference in its entirety.	described below under
	,	Mouse adipocyte cells that	"Hyperproliferative
		may be used according to these	Disorders"). Preferred
		assays are publicly available	indications include blood
		(e.g., through the ATCC).	disorders (e.g., hypertension,
		Exemplary mouse adipocyte	congestive heart failure, blood
-		cells that may be used	vessel blockage, heart disease,
		according to these assays	stroke, impotence and/or as
		include 3T3-L1 cells. 3T3-L1	described below under
		is an adherent mouse	"Immune Activity",
		preadipocyte cell line that is a	"Cardiovascular Disorders",
X-Q-		continuous substrain of 3T3	and/or "Blood-Related
		 fibroblast cells developed	Disorders"), immune disorders
		through clonal isolation and	(e.g., as described below under
		undergo a pre-adipocyte to	"Immune Activity"), neural

ler disorders (e.g., as described below under "Neural Activity and Neurological Diseases"),	and infection (e.g., as described below under	"Infectious Disease").	ndica	is diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,
adipose-like conversion under appropriate differentiation conditions known in the art.																					-				-		
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microvascular disease, hypertension, stroke, and other diseases and disorders as described in the	section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below),	neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g.,	infectious diseases and disorders as described in the "Infectious Diseases" section below (particularly of the urinary tract and skin). An	ghly F obesit is assc litional icatio or alter	weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems
					,

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					including myopathies,
					muscular dystrophy, and/or as
					described herein.
			-		Additional highly preferred
					indications include,
					hypertension, coronary artery
					disease, dyslipidemia,
					gallstones, osteoarthritis,
					degenerative arthritis, eating
					disorders, fibrosis, cachexia,
					and kidney diseases or
					disorders. Preferred
					indications include neoplasms
					and cancer, such as,
					lymphoma, leukemia and
					breast, colon, and kidney
					cancer. Additional preferred
					indications include melanoma,
					prostate, lung, pancreatic,
					esophageal, stomach, brain,
					liver, and urinary cancer.
					Highly preferred indications
					include lipomas and
					liposarcomas. Other preferred
					indications include benign
					dysproliferative disorders and
					pre-neoplastic conditions, such
					as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
,	<b>Н</b> DРUH26	1074	Inhibition of	Reporter Assay: construct	
126			squalene synthetase	contains regulatory and coding	

ic e e e e e e e e e e e e e e e e e e e	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely of polypeptides of the invention (including antibodies of the invention includes a highly preferred embodiment of the invention includes a profession of the invention includes a professio
gene transcription. sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), th contents of which are hereir incorporated by reference ir entirety. Cells were treated with SID supernatants, and SEAP activity was measure after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et Science. 209:497-9 (1980), contents of which are hereir incorporated by reference ir	Activation of Kinase assay. Kinase assays Adipocyte ERK for example an EIk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibod and agonists or antagonists or the invention) to promote or
	HDPUW68 1075
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tiation. A	preferred	e inventio	for	te	A highly	nent of th	s a methoc	ġ,	yte	rnative	mbodime	ncludes a	ing the	, decreasii	g adipocy	ndication	disorders	below un	ders").	ndication	lastic	omas,	/or as	ınder	ve	erred	e blood	pertension	ailure, blc	neart disea
adipocyte differentiation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting adipocyte	differentiation.	preferred embodiment of the	invention includes a method	for stimulating (e.g.,	increasing) adipocyte	activation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting the	activation of (e.g., decreasing)	and/or inactivating adipocytes.	Highly preferred indications	include endocrine disorders	(e.g., as described below under	"Endocrine Disorders")	Highly preferred indications	also include neoplastic	diseases (e.g., lipomas,	liposarcomas, and/or as	described below under	"Hyperproliferative	Disorders"). Preferred	indications include blood	disorders (e.g., hypertension,	congestive heart failure, blood	vessel blockage, heart disease,
adipoc	alterna	empod	include	inhibit	differe	preferr	invent	for stir	increas	activat	highly	of the	metho	activat	and/or	Highly	includ	(e.g., a	"Endo	Highly	also in	disease	liposa	descril	"Hype	Disord	indical	disord	conges	vessel
inhibit cell proliferation,	activation, and differentiation.	Exemplary assays for ERK	kinase activity that may be	used or routinely modified to	test ERK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Le Marchand-	Brustel Y, Exp Clin	Endocrinol Diabetes	107(2):126-132 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	obb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Mouse adipocyte cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC).	Exemplary mouse adipocyte	cells that may be used
ü	ac	<u>—</u>		sn	te	ac	in	an an		as	a	=	B	<u> </u>	10	X	S	ar	4	<u>ن</u>	B	- th		re	Σ	ш	as	<u>e</u>	<u>田</u>	3
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		<u>-</u> .		*	-																									

		according to these assays	stroke, impotence and/or as
		include 3T3-L1 cells   3T3-L1	described below under
		is an adherent mouse	"Immine Activity"
		preadipocyte cell line that is a	"Cardiovascular Disorders".
		continuous substrain of 3T3	and/or "Blood-Related
		fibroblast cells developed	Disorders"), immune disorders
		through clonal isolation and	(e.g., as described below under
		undergo a pre-adipocyte to	"Immune Activity"), neural
	·	adipose-like conversion under	disorders (e.g., as described
		appropriate differentiation	below under "Neural Activity
		conditions known in the art.	and Neurological Diseases"),
	 		and infection (e.g., as
			described below under
			"Infectious Disease").
			A highly preferred indication
			is diabetes mellitus. An
			additional highly preferred
.—.			indication is a complication
	 		associated with diabetes (e.g.,
			diabetic retinopathy, diabetic
			nephropathy, kidney disease
			(e.g., renal failure,
	 		nephropathy and/or other
			diseases and disorders as
			described in the "Renal
			Disorders" section below),
			diabetic neuropathy, nerve
			disease and nerve damage
			(e.g., due to diabetic
	 		neuropathy), blood vessel
			blockage, heart disease, stroke,

impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include
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					-			_	-												10-									

weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. Preferred	indications include neoplasms	and cancer, such as,	lymphoma, leukemia and	breast, colon, and kidney	cancer. Additional preferred	indications include melanoma,	prostate, lung, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer.	Highly preferred indications	•
																							-							
										_																				

					liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
127	HDPUW68	1075	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998). Cullen and Malm.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below).
				Methods in Enzymol 216:362-	boosting a T cell-mediated

immine response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,
368 (1992): Henthorn et al.	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.												
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					metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
127	HDPUW68	1075	Stimulation of Calcium Flux in pancreatic beta cells.	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease

the inver	the invention) to mobilize	(e.g., renal failure,
calcium.	4	nephropathy and/or other
FLPR as		diseases and disorders as
measure		described in the "Renal
Cells not	Cells normally have very low	Disorders" section below),
concentr	concentrations of cytosolic	diabetic neuropathy, nerve
calcium		disease and nerve damage
higher ex	higher extracellular calcium.	(e.g., due to diabetic
Extracell	Extracellular factors can cause	neuropathy), blood vessel
an influx	an influx of calcium, leading to	blockage, heart disease, stroke,
activatio	activation of calcium	impotence (e.g., due to diabetic
responsi	responsive signaling pathways	neuropathy or blood vessel
and after	and alterations in cell	blockage), seizures, mental
functions	functions. Exemplary assays	confusion, drowsiness,
that may	that may be used or routinely	nonketotic hyperglycemic-
modified	modified to measure calcium	hyperosmolar coma,
flux by p	flux by polypeptides of the	cardiovascular disease (e.g.,
invention	invention (including antibodies	heart disease, atherosclerosis,
and agor	and agonists or antagonists of	microvascular disease,
the inver	the invention) include assays	hypertension, stroke, and other
disclosed		diseases and disorders as
Endocrir	Endocrinology, 136(10):4589-	described in the
601 (199	601 (1995);Mogami H, et al.,	"Cardiovascular Disorders"
Endocrir	Endocrinology, 136(7):2960-6	section below), dyslipidemia,
(1995); 1	(1995); Richardson SB, et al.,	endocrine disorders (as
Biochem	Biochem J, 288 (Pt 3):847-51	described in the "Endocrine
(1992);	(1992); and, Meats, JE, et al.,	Disorders" section below),
Cell Cal	Cell Calcium 1989 Nov-	neuropathy, vision impairment
Dec;10(	Dec;10(8):535-41 (1989), the	(e.g., diabetic retinopathy and
contents	contents of each of which is	blindness), ulcers and impaired
herein in	herein incorporated by	wound healing, and infection

HDPUW68 1075		Failcreatic ceits that may be	disorders as described in the
HDPUW68		used according to these assays	"Infectious Diseases" section
HDPUW68		are publicly available (e.g.,	below, especially of the
HDPUW68		through the ATCC) and/or	urinary tract and skin), carpal
HDPUW68		may be routinely generated.	tunnel syndrome and
HDPUW68		Exemplary pancreatic cells that	Dupuytren's contracture).
HDPUW68		may be used according to these	An additional highly preferred
HDPUW68		assays include HITT15 Cells.	indication is obesity and/or
HDPUW68		HITT15 are an adherent	complications associated with
HDPUW68		epithelial cell line established	obesity. Additional highly
HDPUW68		from Syrian hamster islet cells	preferred indications include
HDPUW68		transformed with SV40. These	weight loss or alternatively,
HDPUW68		cells express glucagon,	weight gain. Aditional
HDPUW68		somatostatin, and	highly preferred indications are
HDPUW68		glucocorticoid receptors. The	complications associated with
HDPUW68		cells secrete insulin, which is	insulin resistance.
HDPUW68		stimulated by glucose and	
HDPUW68		glucagon and suppressed by	
HDPUW68		somatostatin or	
HDPUW68		glucocorticoids. ATTC# CRL-	
HDPUW68		1777 Refs: Lord and	
HDPUW68		Ashcroft. Biochem. J. 219:	
HDPUW68		547-551; Santerre et al. Proc.	
HDPUW68		Natl. Acad. Sci. USA 78:	
HDPUW68		4339-4343, 1981.	
	Activation of	Kinase assay. Kinase assays,	A highly preferred
	Skeletal Mucle Cell	for example an GSK-3 kinase	embodiment of the invention
	PI3 Kinase	assay, for PI3 kinase signal	includes a method for
	Signalling Pathway	transduction that regulate	increasing muscle cell survival
		glucose metabolism and cell	An alternative highly preferred

includes a m decreasing n survival.  embodiment includes a m simulating a proliferation embodiment cell prolifera a m inhibiting m inhibiting m inhibiting m proliferation embodiment cell proliferation embodiment cell proliferation embodiment cell proliferation method for second the invention method for second fiftenent specific embodiment cell different specific embodiment cell different specific embodiment cell different specific embodiment specific embodiment cell different specific embodiment specific embodiment cell different specific embodic inhibited	
survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for PI3 kinase activity that may be used or routinely modified to test PI3 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Nikoulina et al., Diabetes 48(8):1662-1666 (1999), the contents of each of which are herein incorporated by reference in its entirety. Rat myoblast cells that may be used according to these assays are publicly available (e.g., through the ATCC).	survivial are well-known in the art and may be used or routinely modificat to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for Pl3 kinase activity that may be used or routinely modified to test Pl3 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Forrer et al., Biol (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et al., Diabetes 48(8):1662-1666 (1999), the contents of each of which are herein incorporated by reference in its entirety.  Rat myoblast cells that may be used according to these assays are publicly available (e.g., through the ATCO).

indications include disorders of the musculoskeletal system. Preferred indications include	neoplastic diseases (e.g., as described below under	"Hyperproliferative	Disorders"), endocrine	disorders (e.g., as described	below under "Endocrine	Disorders"), neural disorders	(e.g., as described below under	"Neural Activity and	Neurological Diseases"), blood	disorders (e.g., as described	below under "Immune	Activity", "Cardiovascular	Disorders", and/or "Blood-	Related Disorders"), immune	disorders (e.g., as described	below under "Immune	Activity"), and infection (e.g.,	as described below under	"Infectious Disease"). A	highly preferred indication is	diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,
that may be used according to these assays include L6 cells. L6 is an adherent rat myoblast	cell line, isolated from primary cultures of rat thigh muscle.	that fuses to form	multinucleated myotubes and	striated fibers after culture in	differentiation media.																						
		-																									
																				-							

_				nephropath	nephropathy and/or other
				diseases an	diseases and disorders as
				described in	described in the "Renal
_				Disorders"	Disorders" section below),
		•		diabetic neu	diabetic neuropathy, nerve
				disease and	disease and nerve damage (e.g.,
				due to diab	due to diabetic neuropathy),
				blood vesse	blood vessel blockage, heart
				disease, str	disease, stroke, impotence
				(e.g., due to diabetic	diabetic
				neuropathy	neuropathy or blood vessel
				blockage),	blockage), seizures, mental
				confusion,	confusion, drowsiness,
-	-			nonketotic	nonketotic hyperglycemic-
				hyperosmolar coma,	lar coma,
				cardiovascu	cardiovascular disease (e.g.,
				heart diseas	heart disease, atherosclerosis,
	λ	<u>.</u>		microvascu	microvascular disease,
		<del>-</del>		hypertensio	hypertension, stroke, and other
				diseases an	diseases and disorders as
				described in the	n the
				"Cardiovas	"Cardiovascular Disorders"
				section belo	section below), dyslipidemia,
				endocrine d	endocrine disorders (as
		-		described in	described in the "Endocrine
		_		Disorders"	Disorders" section below),
		-		neuropathy	neuropathy, vision impairment
	•,	_		(e.g., diaber	(e.g., diabetic retinopathy and
		-		blindness),	blindness), ulcers and impaired
		<del></del>		wound heal	wound healing, infections
				(e.g., infect	(e.g., infectious diseases and

disorders as described in the	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additonal highly preferred	indications are disorders of the	musculoskeletal system	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include: myopathy,	atrophy, congestive heart	failure, cachexia, myxomas,	fibromas, congenital	cardiovascular abnormalities,	heart disease, cardiac arrest,	heart valve disease, and	11: 11: 11:
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preferred indications include neoplasms and cancer, such as, rhabdomyoma, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as
preferred i neoplasms rhabdomy rhabdosar esophagea urinary ca indication lung, colo and liver preferred i benign dy disorders i conditions hyperplasi dysplasia.	incining in the state of the st
	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that
	Activation of transcription through NFKB response element in immune cells (such as T-cells).
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	may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these in the set of th	described below). An additional highly preferred indication is infection (e.g., AIDS, and/or an infectious disease as described below under "Infectious Disease"). Highly preferred indications include neoplastic diseases (e.g., melanoma, leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as,melanoma, renal cell carcinoma, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for	
	 assays include the SUPT cell line, which is a suspension	example, hyperplasia, metaplasia, and/or dysplasia.	
	culture of IL-2 and IL-4 responsive T cells.	Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia,	
		Hodgkin's disease, acute	

lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease,	sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and allergy.	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g.,
		This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to
		Activation of transcription through GATA-3 response element in immune cells (such as mast cells).
		1077
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	regulate GATA3 transcription	rheumatoid arthritis, systemic
		lupus erythematosis, multiple
	expression of mast cell genes	sclerosis and/or as described
	 important for immune response	below) and
	 development. Exemplary	immunodeficiencies (e.g., as
	assays for transcription	described below). Preferred
	through the GATA3 response	indications include neoplastic
	element that may be used or	diseases (e.g., leukemia,
	 routinely modified to test	lymphoma, melanoma,
	GATA3-response element	prostate, breast, lung, colon,
	activity of polypeptides of the	pancreatic, esophageal,
	 invention (including antibodies	stomach, brain, liver, and
	and agonists or antagonists of	urinary tract cancers and/or as
	 the invention) include assays	described below under
	disclosed in Berger et al., Gene	"Hyperproliferative
	 66:1-10 (1998); Cullen and	Disorders"). Other preferred
	Malm, Methods in Enzymol	indications include benign
	 216:362-368 (1992); Henthorn	dysproliferative disorders and
	et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
	85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
	 et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
	Quant Biol 64:563-571 (1999);	Preferred indications include
	Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
_	J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
	(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
	Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
	Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
	14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
	contents of each of which are	lymphoma, arthritis, AIDS,
	herein incorporated by	granulomatous disease,
	reference in its entirety. Mast	inflammatory bowel disease,

sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	
cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be
	Proliferation of preadipose cells (such as 3T3-L1 cells)
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	HDPVW11
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	Highly preferred indications include asthma, allergy, hypersensitivity reactions, inflammation, and inflammatory disorders.  Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s
used to measure the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127-133 (1974), which is herein incorporated by reference in its entirety.	Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis.  Exemplary assays for JNK
	Activation of JNK Signaling Pathway in immune cells (such as eosinophils).
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	HDPWN93
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		kinase activity that may be	disease, multiple sclerosis
		used or routinely modified to	and/or as described below),
		test JNK kinase-induced	immunodeficiencies (e.g., as
		activity of polypeptides of the	described below). Highly
	1	invention (including antibodies	preferred indications also
		and agonists or antagonists of	include boosting or inhibiting
		the invention) include the	immune cell proliferation.
		assays disclosed in Forrer et	Preferred indications include
		al., Biol Chem 379(8-9):1101-	neoplastic diseases (e.g.,
		1110 (1998); Gupta et al., Exp	leukemia, lymphoma, and/or as
		Cell Res 247(2): 495-504	described below under
	_	(1999); Kyriakis JM, Biochem	"Hyperproliferative
		Soc Symp 64:29-48 (1999);	Disorders"). Highly preferred
		Chang and Karin, Nature	indications include boosting an
		410(6824):37-40 (2001); and	eosinophil-mediated immune
		Cobb MH, Prog Biophys Mol	response, and suppressing an
		Biol 71(3-4):479-500 (1999);	eosinophil-mediated immune
		the contents of each of which	response.
		are herein incorporated by	
		reference in its entirety.	
		Exemplary cells that may be	
		used according to these assays	
		include eosinophils.	
		Eosinophils are important in	
		the late stage of allergic	
3.1		reactions; they are recruited to	
		tissues and mediate the	
		inflammatory response of late	
		stage allergic reaction.	
		Moreover, exemplary assays	
		that may be used or routinely	

modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate signal transduction, cell proliferation, activation, or	apoptosis in eosinophils include assays disclosed and/or cited in: Zhang JP, et al., "Role of caspases in dexamethasone-induced apoptosis and activation of c-Jun NH2-terminal kinase and p38 mitogen-activated protein	kinase in human eosinophils" Clin Exp Immunol; Oct; 122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils" J Exp Med; Feb 2;187(3):415-25 (1998); J	Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N- terminal kinase and failure of

	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for inhibiting endothelial cells. An endothelial cells. An alternative highly preferred
	A highly preferred embodiment of the invincludes a method for stimulating endothelia growth. An alternative preferred embodiment invention includes a m for inhibiting endothelia growth. A highly perpoliferation. An alterninglally proliferation. An alterninglally proliferation. An alterninglally preferred embo of the invention include method for inhibiting endothelial cell prolife A highly preferred embodiment of the invincludes a method for stimulating apoptosis endothelial cells. An alternative highly preferred embodiment of the invincludes a method for stimulating apoptosis endothelial cells. An alternative highly preferred
prednisolone to inhibit JUN N-terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et
·	Activation of Endothelial Cell p38 or JNK Signaling Pathway.
	1078
	HDPWN93
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embodiment of the invention includes a method for inhibiting (e.g., decreasing) apoptosis of endothelial cells. A highly preferred	embodiment of the invention includes a method for stimulating (e.g., increasing) endothelial cell activation. An	embodiment of the invention includes a method for inhibiting (e.g., decreasing) the activation of and/or	inactivating endothelial cells. A highly preferred embodiment of the invention includes a method for	stimulating angiogenisis. An alternative highly preferred embodiment of the invention includes a method for inhibiting angiogenesis. A highly preferred embodiment	of the invention includes a method for reducing cardiac hypertrophy. An alternative highly preferred embodiment of the invention includes a method for inducing cardiac hypertrophy.
al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999);	Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999);	are herein incorporated by reference in its entirety.  Endothelial cells that may be used according to these assays	are publicly available (e.g., through the ATCC).  Exemplary endothelial cells that may be used according to	these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that	include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.

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le	r <b>^</b>			Jo		(e.g., heart disease, congestive				ar	S	Ħ	hy,				hemodynamic overload, and/or		<u>''</u>	JS		nic		S	35	sels			<b>&gt;</b>	ıgt
preferred indications include	neoplastic diseases (e.g., as			Disorders"), and disorders of	em	gesi	heart failure, hypertension,		lar	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	liac	al		l, an	ler	"Cardiovascular Disorders").	Highly preferred indications	<u>.</u>	endothelial and/or angiogenic	္ပည	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	the	ins	and/or lymphatics). Highly	preferred are indications that
ıs in	(e.g	ıder	<b>(1)</b>	sord	syst	200	tens		alvu	/enti	scle	vas	phr	carc	ardi		rloac	un,	isor	ndica	ula	angi	tem	it ve	ellit	the	s of	, ve	Η.	atio
ation	ases	un ∧	ative	id di	ılar	ase,	yper		y, V	eft v	hero	otic	ic ne	unt,	1yoc	nic	ove	low	ar D	ed ir	vasc	I/or	Sys	affec	ss m	s of	ch a	aries	tics)	ndic
ldic.	dise	elor	lifer	), an	ascı	dise	e, h	sis,	path	on, l	n, at	scle	abet	c sh	y, n	chrc	mic	d be	scul	ferre	rdio	lanc	e is	hat a	bete	ease	s, su	pilla	ipha	re ii
ed ir	stic (	described below under	"Hyperproliferative	ers"	the cardiovascular system	eart	ailur	aortic stenosis,	cardiomyopathy, valvular	itati	ctio	ero	, di	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	ynai	as described below under	ovas	pre ,	include cardiovascular,	elia	disorders (e.g., systemic	ers t	s dia	dis	themselves, such as of the	arteries, capillaries, veins	lym,	e pa
ferr	opla	Scrib	ypei	sord	car	g., h	art fa	rtic s	dio.	gurg	sfun	dath	ease	raca	perti	arct	mod	desc	ardi	ghly	lude	doth	sord	sord	ch a	ell as	sms	erie	d/or ^	efen
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stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization.	Highly preferred indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal disorders. Highly preferred indications	include neoplasms and cancer, such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma,	angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such
·			

as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as, atheroscierosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud's disease and Reynaud's disease and Reynaud's phenomenom, aneurysms, reschoosis; varous and lymphatic disorders such as thrombophebitis, and hymphatic disorders such as peripheral vascular disorders such as peripheral vascular disorders such as and cancer. Highly preferred indications also include traums auch as wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from balloon angiophasty, and atheroschlerotic lesions), implant fixation, searning, ischemia reperfusion injury, theumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal diseases, renal disease, re

Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders,	vascularitis, lymph angiogenesis, sexual disorders, age-related macular degeneration, and treatment /prevention of endometriosis and related conditions.	Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease.	blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or	Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple	sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include
Addit indica graft 1 other and co	vascu angio age-re degen /preve	Addit indica heart heart heart vascu	blood describing "Imm"	Caro Prefer autoir rheun Iupus	sclerc belov immu descr prefe

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inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	A highly preferred embodiment of the invention includes a method for increasing adipocyte survival An alternative highly preferred embodiment of the invention includes a method for decreasing adipocyte survival. A preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting
	Kinase assay. Kinase assays, for example an GSK-3 assays, for PI3 kinase signal transduction that regulate glucose metabolism and cell survival are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for PI3 kinase activity that may be used or routinely modified to test PI3 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110
	Activation of Adipocyte P13 Kinase Signalling Pathway
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	HDPWU34
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diabetes (e.g., diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage (e.g.,	due to diabetic neuropathy),	blood vessel blockage, heart	disease, stroke, impotence	(e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment
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(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and	disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal	tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or	complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional	s assocance. ance. ighly predisocatel systems	including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis,

HDPWU34 1079 Activation of transcription through GAS response element in immune cells (such as eosinophils).
as eosinophi

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rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis	and/or as described below), immunodeficiencies (e.g., as	described below), boosting an	response and, alternatively,	suppressing an eosinophil-	mediated immune response.						_															
via STAT transcription factors) involved in a wide variety of cell functions. Exemplary	assays for transcription through the GAS response	element that may be used or	GAS-response element activity	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995); the	contents of each of which are	herein incorporated by	reference in its entirety.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of
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the invention) to activate or	inhibit activation of immune	cells include assays disclosed	and/or cited in: Mayumi M.,	"EoL-1, a human eosinophilic	cell line" Leuk Lymphoma;	Jun;7(3):243-50 (1992);	Bhattacharya S, "Granulocyte	macrophage colony-	stimulating factor and	interleukin-5 activate STAT5	and induce CIS1 mRNA in	human peripheral blood	eosinophils" Am J Respir Cell	Mol Biol; Mar;24(3):312-6	(2001); and, Du J, et al.,	"Engagement of the CrkL	adapter in interleukin-5	signaling in eosinophils" J Biol	Chem; Oct 20;275(42):33167-	75 (2000); the contents of each	of which are herein	incorporated by reference in its	entirety. Exemplary cells that	may be used according to these	assays include eosinophils.	Eosinophils are a type of	immune cell important in the	late stage of allergic reactions;	they are recruited to tissues	and mediate the inflammtory
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response of late stage allergic reaction. Increases in GAS mediated transcription in eosinophils is typically a result of STAT activation, normally a direct consequence of interleukin or other cytokine receptor stimulation (e.g. IL3, IL5 or GMCSF).	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically
	Proliferation of preadipose cells (such as 3T3-L1 cells)
	1079
	HDPWU34
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active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127-133 (1974), which is herein incorporated by reference in its entirety.	Assays for activation of transcription are well-known in the art and may be used and routinely modified to assess ability of polypeptides of the invention to inhibit or activate transcription. An example of such an assay follows: Cells were pretreated with SID supernatants or controls for 15-18 hours. SEAP activity was measured after 48 hours.  LS174T is an epithelial colon adenocarcinoma cell line. Its tumourigenicity in nude mice make cell line LS174T a model for studies on the mechanism of synthesis and secretion of specific tumoral markers in
active ce mouse pi is a conti 3T3 fibro through were diff adipose- used in t H and M 133 (197) incorpor- entirety.	Assay transc the art routin ability invent transc such a were I superr 18 hor measu LS174 adeno tumou make for stu of syn specif
	Activation of Transcription
	1079
	HDPWU34
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				colon cancer. See, Patan et al., Circ Res, 89(8):732-39 (2001), the contents of which are herein incorporated by reference in its entirety	
132	нронроз	1080	Production of IL-10 and activation of T-cells.	Assays for production of IL-10 and activation of T-cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit production of IL-10 and/or activation of T-cells. Exemplary assays that may be used or routinely modified to assess the ability of polypeptides and antibodies of the invention) (including agonists or antagonists of the invention) to modulate IL-10 production and/or T-cell proliferation include, for example, assays such as disclosed and/or cited in: Robinson, DS, et al., "Th-2 cytokines in allergic disease"	Highly preferred indications include allergy and asthma. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response.
				Br Med Bull; 56 (4): 956-968 (2000), and Cohn, et al., "T-	

	Highly preferred indications include diabetes, myopathy, muscle cell atrophy, cancers of muscle (such as, rhabdomyoma, and
helper type 2 cell-directed therapy for asthma" Pharmacology & Therapeutics; 88: 187-196 (2000); the contents of each of which are herein incorporated by reference in their entirety. Exemplary cells that may be used according to these assays include Th2 cells. IL10 secreted from Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and activation of Th2 cells play a major role in the initiation and cutvation of Th2 cells play a major role culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.	Assays for muscle cell proliferation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of
	Myoblast cell proliferation
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The III	me invention (including	maddosarcomaj,
antibo	antibodies and agonists or	cardiovascular disorders (such
antago	antagonists of the invention) to	as congestive heart failure,
stimul	stimulate or inhibit myoblast	cachexia, myxomas, fibromas,
cell pr	cell proliferation. Exemplary	congenital cardiovascular
assays	assays for myoblast cell	abnormalities, heart disease,
prolife	proliferation that may be used	cardiac arrest, heart valve
or rou	or routinely modified to test	disease, vascular disease, and
activit	activity of polypeptides and	also as described below under
antibo	antibodies of the invention	"Cardiovascular Disorders"),
(inclu	(including agonists or	stimulating myoblast
antago	antagonists of the invention)	proliferation, and inhibiting
includ	include, for example, assays	myoblast proliferation.
disclo	disclosed in: Soeta, C., et al.	
"Possi	"Possible role for the c-ski	
 gene i	gene in the proliferation of	
myoge	myogenic cells in regenerating	
skelet	skeletal muscles of rats" Dev	
 Grow	Growth Differ Apr;43(2):155-	
 64 (20	64 (2001); Ewton DZ, et al.,	
 "IGF	"IGF binding proteins-4, -5	
 - and -6	and -6 may play specialized	
roles	roles during L6 myoblast	
 prolife	proliferation and	
 differe	differentiation" J Endocrinol	
Mar;1	Mar;144(3):539-53 (1995);	
 and, P	and, Pampusch MS, et	
 al.,"E	al.,"Effect of transforming	
growt	growth factor beta on	
 prolife	proliferation of L6 and	
embry	embryonic porcine myogenic	

				cells" J Cell Physiol Jun; 143(3):524-8 (1990); the contents of each of which are herein incorporated by reference in their entirety. Exemplary myoblast cells that may be used according to these assays include the rat myoblast L6 cell line. Rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation modia	
134	HDTBP04	1082	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as

	proteins produced by a large	"Immune Activity", "Blood-
 •	variety of cells where the	Related Disorders", and/or
	expression level is strongly	"Cardiovascular Disorders"),
	regulated by cytokines, growth	and infection (e.g., as
	factors, and hormones are well	described below under
	known in the art and may be	"Infectious Disease"). Highly
	used or routinely modified to	preferred indications include
	assess the ability of	autoimmune diseases (e.g.,
	polypeptides of the invention	rheumatoid arthritis, systemic
	(including antibodies and	lupus erythematosis, multiple
 •	agonists or antagonists of the	sclerosis and/or as described
**********	invention) to mediate	below) and
	immunomodulation and	immunodeficiencies (e.g., as
 	differentiation and modulate T	described below). Highly
 	cell proliferation and function.	preferred indications also
 	Exemplary assays that test for	include boosting a B cell-
	immunomodulatory proteins	mediated immune response
 	evaluate the production of	and alternatively suppressing a
-	cytokines, such as IL-6, and	B cell-mediated immune
	the stimulation and	response. Highly preferred
 	upregulation of T cell	indications include
	proliferation and functional	inflammation and
 	activities. Such assays that	inflammatory
 	may be used or routinely	disorders.Additional highly
	modified to test	preferred indications include
 	immunomodulatory and	asthma and allergy. Highly
	diffferentiation activity of	preferred indications include
	polypeptides of the invention	neoplastic diseases (e.g.,
	(including antibodies and	myeloma, plasmacytoma,
	agonists or antagonists of the	leukemia, lymphoma,
	invention) include assays	melanoma, and/or as described

disclosed in Miraglia et al., J Biomolecular Screening 4:193- 204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	discle Biom 204(1 "Lym appro (2000 Immu (1997 which be us assay techn other Hum antigs suspe when and/o
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					diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
	HDTBP04	1082	Production of	MCP-1 FMAT. Assays for	A highly preferred
134			MCP-1	immunomodulatory proteins	embodiment of the invention
				that are produced by a large	includes a method for
				variety of cells and act to	stimulating (e.g., increasing)
	_			induce chemotaxis and	MCP-1 production. An
				activation of monocytes and T	alternative highly preferred
				cells are well known in the art	embodiment of the invention
				and may be used or routinely	includes a method for
				modified to assess the ability	.2
				of polypeptides of the	MCP-1 production. A highly
				invention (including antibodies	preferred indication is
				and agonists or antagonists of	infection (e.g., an infectious
				the invention) to mediate	disease as described below
				immunomodulation, induce	under "Infectious Disease").
				chemotaxis, and modulate	Additional highly preferred
				immune cell activation.	indications include
				Exemplary assays that test for	inflammation and
				immunomodulatory proteins	inflammatory disorders.
				evaluate the production of cell	Preferred indications include
				surface markers, such as	blood disorders (e.g., as
				monocyte chemoattractant	described below under
				protein (MCP), and the	"Immune Activity", "Blood-
				activation of monocytes and T	Related Disorders", and/or
				cells. Such assays that may be	"Cardiovascular Disorders").

			used or routinely modified to	Highly preferred indications
	-	~- <del></del>	test immunomodulatory and	include autoimmune diseases
			diffferentiation activity of	(e.g., rheumatoid arthritis,
-			polypeptides of the invention	systemic lupus erythematosis,
			(including antibodies and	multiple sclerosis and/or as
			agonists or antagonists of the	described below) and
			invention) include assays	immunodeficiencies (e.g., as
	-		disclosed in Miraglia et al., J	described below). Preferred
			Biomolecular Screening 4:193-	indications also include
			204(1999); Rowland et al.,	anemia, pancytopenia,
			"Lymphocytes: a practical	leukopenia, thrombocytopenia,
			approach" Chapter 6:138-160	Hodgkin's disease, acute
			(2000); Satthaporn and	lymphocytic anemia (ALL),
		-,-	Eremin, J R Coll Surg Ednb	plasmacytomas, multiple
			45(1):9-19 (2001); and	myeloma, Burkitt's lymphoma,
	*.		Verhasselt et al., J Immunol	arthritis, AIDS, granulomatous
			158:2919-2925 (1997), the	disease, inflammatory bowel
			contents of each of which are	disease, sepsis, neutropenia,
			herein incorporated by	neutrophilia, psoriasis,
			reference in its entirety.	suppression of immune
			Human dendritic cells that may	reactions to transplanted
			be used according to these	organs and tissues,
			assays may be isolated using	hemophilia, hypercoagulation,
			techniques disclosed herein or	diabetes mellitus, endocarditis,
			otherwise known in the art.	meningitis (bacterial and
			Human dendritic cells are	viral), Lyme Disease, asthma,
			antigen presenting cells in	and allergy Preferred
			suspension culture, which,	indications also include
			when activated by antigen	neoplastic diseases (e.g.,
			and/or cytokines, initiate and	leukemia, lymphoma, and/or as
			upregulate T cell proliferation	described below under

			and functional activities.	"Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
HDTBP04	1082	Production of ICAM-1	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke

	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention
each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Induction of apoptosis in endothelial cells supporting the vasculature of tumors is associated with tumor regression due to loss of tumor blood supply. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase
	Endothelial Cell Apoptosis
	1083
	HDTDQ23
	135

apoptosis activity of	includes a method for
polypeptides of the invention	stimulating apoptosis of
(including antibodies and	endothelial cells. An
agonists or antagonists of the	alternative highly preferred
invention) include the assays	embodiment of the invention
disclosed in Lee et al., FEBS	includes a method for
Lett 485(2-3): 122-126 (2000);	inhibiting (e.g., decreasing)
Nor et al., J Vasc Res 37(3):	apoptosis of endothelial cells.
209-218 (2000); and Karsan	A highly preferred
and Harlan, J Atheroscler	embodiment of the invention
Thromb 3(2): 75-80 (1996);	includes a method for
the contents of each of which	stimulating angiogenisis. An
are herein incorporated by	alternative highly preferred
reference in its entirety.	embodiment of the invention
Endothelial cells that may be	includes a method for
used according to these assays	inhibiting angiogenesis. A
are publicly available (e.g.,	highly preferred embodiment
through commercial sources).	of the invention includes a
Exemplary endothelial cells	method for reducing cardiac
that may be used according to	hypertrophy. An alternative
these assays include bovine	highly preferred embodiment
aortic endothelial cells	of the invention includes a
(bAEC), which are an example	method for inducing cardiac
of endothelial cells which line	hypertrophy. Highly
blood vessels and are involved	preferred indications include
in functions that include, but	neoplastic diseases (e.g., as
are not limited to,	described below under
angiogenesis, vascular	"Hyperproliferative
permeability, vascular tone,	Disorders"), and disorders of
and immune cell extravasation.	the cardiovascular system
	(e.g., heart disease, congestive

heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis	and atherosclerotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or ac described below, under	"Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels	themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred indications include antiangiogenic activity
			-

to treat solid tumors,	leukemias, and national disorders	sarcoma, and relinal disolders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory
			_												-															
								***		3.																				

vasculitides, Reynaud"s disease and Reynaud"s phenomenom, aneurysms, restenosis; venous and	lymphatic disorders such as thrombophlebitis, lymphangitis, and lymphedema; and other	vascular disorders such as peripheral vascular disease, and cancer. Highly preferred indications also	include trauma such as wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from	balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury,	cerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis.	Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders,

age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	preferred indications include	inflammation and	inflammatory disorders (such	as acute and chronic	inflammatory diseases, e.g.,	inflammatory bowel disease	and Crohn's disease), and pain	management.
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	HDTD023	1083	Stimulation of	Assays for measuring calcium	A highly preferred
135			Calcium Flux in	flux are well-known in the art	indication is diabetes mellitus.
			pancreatic beta	and may be used or routinely	An additional highly preferred
			cells.	modified to assess the ability	indication is a complication
				of polypeptides of the	associated with diabetes (e.g.,
				invention (including antibodies	diabetic retinopathy, diabetic
				and agonists or antagonists of	nephropathy, kidney disease
				the invention) to mobilize	(e.g., renal failure,
				calcium. For example, the	nephropathy and/or other
				FLPR assay may be used to	diseases and disorders as
				measure influx of calcium.	described in the "Renal
				Cells normally have very low	Disorders" section below),
				concentrations of cytosolic	diabetic neuropathy, nerve
				calcium compared to much	disease and nerve damage
				higher extracellular calcium.	(e.g., due to diabetic
				Extracellular factors can cause	neuropathy), blood vessel
				an influx of calcium, leading to	blockage, heart disease, stroke,
				activation of calcium	impotence (e.g., due to diabetic
				responsive signaling pathways	neuropathy or blood vessel
				and alterations in cell	blockage), seizures, mental
		2.22		functions. Exemplary assays	confusion, drowsiness,
				that may be used or routinely	nonketotic hyperglycemic-
				modified to measure calcium	hyperosmolar coma,
				flux by polypeptides of the	cardiovascular disease (e.g.,
		-		invention (including antibodies	heart disease, atherosclerosis,
				and agonists or antagonists of	microvascular disease,
			-	the invention) include assays	hypertension, stroke, and other
				disclosed in: Satin LS, et al.,	diseases and disorders as
				Endocrinology, 136(10):4589-	described in the
				601 (1995);Mogami H, et al.,	"Cardiovascular Disorders"
				Endocrinology, 136(7):2960-6	section below), dyslipidemia,

endocrine disorders (as described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Aditional	highly preferred indications are	complications associated with	insulin resistance.							
(1995); Richardson SB, et al., Biochem J, 288 ( Pt 3):847-51	(1992); and, Meats, JE, et al.,	Cell Calcium 1989 Nov-	Dec;10(8):535-41 (1989), the	contents of each of which is	herein incorporated by	reference in its entirety.	Pancreatic cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary pancreatic cells that	may be used according to these	assays include HITT15 Cells.	HITT15 are an adherent	epithelial cell line established	from Syrian hamster islet cells	transformed with SV40. These	cells express glucagon,	somatostatin, and	glucocorticoid receptors. The	cells secrete insulin, which is	stimulated by glucose and	glucagon and suppressed by	somatostatin or	glucocorticoids. ATTC# CRL-	1777 Refs: Lord and	Ashcroft. Biochem. J. 219:	547-551; Santerre et al. Proc.
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	A highly preferred	embodiment of the invention	includes a method for	stimulating the production of	IFNg. An alternative highly	preferred embodiment of the	invention includes a method	for inhibiting the production of	IFNg. Highly preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders",	"Hyperproliferative Disorders"	(e.g. cancer/tumorigenesis)	and/or "Cardiovascular	Disorders"), and infection	(e.g., viral infections,	tuberculosis, infections	associated with chronic	granulomatosus disease and	malignant osteoporosis, and/or	as described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune disease (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple
Natl. Acad. Sci. USA 78: 4339-4343, 1981.	IFNgamma FMAT. IFNg	plays a central role in the	immune system and is	considered to be a	proinflammatory cytokine.	IFNg promotes TH1 and	inhibits TH2; promotes IgG2a	and inhibits IgE; induces	macrophage activation; and	increases MHC expression.	Assays for immunomodulatory	proteins produced by T cells	and NK cells that regulate a	variety of inflammatory	activities and inhibit TH2	helper cell functions are well	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, regulate	inflammatory activities,	modulate TH2 helper cell	function, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays
	Production of	IFNgamma using	Natural Killer cells				_																	-					
	1084																			200									
	HDTEK44																				-								
		136												11															

that test for	sclerosis and/or as described
immunomodulatory proteins	below), immunodeficiency
evaluate the production of	(e.g., as described below),
cytokines, such as Interferon	boosting a T cell-mediated
gamma (IFNg), and the	immune response, and
 activation of T cells. Such	suppressing a T cell-mediated
assays that may be used or	immune response, boosting
routinely modified to test	antibody-dependent immune
immunomodulatory activity of	responses, suppressing
polypeptides of the invention	antibody-dependent immune
(including antibodies and	responses, boosting innate
agonists or antagonists of the	immunity and immune
invention) include the assays	responses, and suppressing
disclosed in Miraglia et al., J	innate immunity and immune
 Biomolecular Screening 4:193-	responses. Additional highly
204 (1999); Rowland et al.,	preferred indications include
"Lymphocytes: a practical	inflammation and
approach" Chapter 6:138-160	inflammatory disorders.
(2000); Gonzalez et al., J Clin	Additional preferred
Lab Anal 8(5):225-233 (1995);	indications include idiopathic
Billiau et al., Ann NY Acad	pulmonary fibrosis. Highly
Sci 856:22-32 (1998); Boehm	preferred indications include
et al., Annu Rev Immunol	neoplastic diseases (e.g.,
15:749-795 (1997), and	leukemia, lymphoma,
Rheumatology (Oxford)	melanoma, and/or as described
38(3):214-20 (1999), the	below under
contents of each of which are	"Hyperproliferative
herein incorporated by	Disorders"). Highly preferred
reference in its entirety.	indications include neoplasms
Natural Killer (NK) cells that	and cancers, such as, for
may be used according to these	example, leukemia, lymphoma,

(e.g., through the ATCC) or may be isolated using techniques disolosed herein or live otherwise known in the art.  Natural killer (NK) cells are large granular lymphocytes distant have cytotoxic activity but condo bind antigen. NK cells exsolve and also prepared of the have cytotoxic activity but condominate in the killing of tumor cells and also prepared of the killing of tumor cells and also prepared of the killing of tumor cells and also prepared of the killing of tumor cells and also prepared of the ceceptors, leading to cell.  In the condomination of the cells of th					assavs are nublicly available	melanoma, and prostate,
may be isolated using techniques disclosed herein or otherwise known in the art. Natural killer (NK) cells are large granular lymphocytes district that have cytotoxic activity but cot do bind antigen. NK cells show antibody-independent me killing of tumor cells and also recognize antibody bound on and recognize antibody bound on and receptors, leading to cell- Ho mediated cytotoxicity. In mediated cytotox					(e.g., through the ATCC) or	breast, lung, colon, pancreatic,
techniques disclosed herein or otherwise known in the art.  Natural killer (NK) cells are ber large granular lymphocytes (that have cytotoxic activity but conditions) and antigen. NK cells show antibody-independent met killing of tumor cells and also preceoping antibody bound on and target cells, via NK Fc learned and antigent cell-homediated cytotoxicity. If the mediated cytotoxicity is plain antibody and antibody antibody.  HDTEN81 1085 CD152 in Human T cells activation of Assays for the activation assays assays for the activation assays assays assays for the activation assays as a say assays as a say as a sa					may be isolated using	esophageal, stomach, brain,
otherwise known in the art. Pre Natural killer (NK) cells are large granular lymphocytes distributed by that have eytotoxic activity but condo bind antigen. NK cells exists show antibody-independent me killing of tumor cells and also preceding of unmor cells and also preceding of unmor cells and also preceding to cell. Ho mediated cytotoxicity. If the mediated cytotoxicity is plain that the cells are cells and also precedent and and the cells are cells and also precedent and and the cells are cells and also precedent and and the cells are cells are cells and also precedent and and and the cells are					techniques disclosed herein or	liver and urinary cancer. Other
Natural killer (NK) cells are ber large granular lymphocytes dis that have cytotoxic activity but con do bind antigen. NK cells exs show antibody-independent me killing of tumor cells and also preceding and antigen cells and also receptors, leading to cell-homediated cytotoxicity. In my art mediated cytotoxicity. In the ceptors is also and also and antigen cells and also are ceptors, leading to cell-lympath. In the control of the ceptors is also antigen cells and also are cells and also are cells. In the ceptors is also antigen cells and also are cells and also are cells. In the cells are cells are cells and are cells and are cells. In the cells are cells are cells are cells are cells are cells. In the cells are cells are cells are cells are cells are cells. In the cells are cells are cells are cells are cells are cells. Assays for the activation of cells.					otherwise known in the art.	preferred indications include
large granular lymphocytes district that have cytotoxic activity but condition of the cytotoxicity.  In the cytotoxic activity but condition of the cytotoxicity of the cytotoxicity.  In the cytotoxicity of					Natural killer (NK) cells are	benign dysproliferative
that have cytotoxic activity but con do bind antigen. NK cells show antibody-independent me killing of tumor cells and also recognize antibody bound on and target cells, via NK Fc leureceptors, leading to cell- Ho mediated cytotoxicity. If you mediated cytotoxicity. If you have the discontinuous and the company of the cells leading to cells. The property of the cells and the company of the cells and the contraction of the cells.					large granular lymphocytes	disorders and pre-neoplastic
do bind antigen. NK cells exa show antibody-independent me killing of tumor cells and also Pre recognize antibody bound on and target cells, via NK Fc leu receptors, leading to cell- Ho mediated cytotoxicity. In plan and target cells, via NK Fc leu receptors, leading to cell- Ho mediated cytotoxicity. In plan and target cells and target cells and target cells and target cells. Via NK Fc leading to cell- Horrest loss of the activation of Assays for the activation of leading shows a signal and target cells.					that have cytotoxic activity but	conditions, such as, for
show antibody-independent me killing of tumor cells and also Pre recognize antibody bound on and target cells, via NK Fc leu receptors, leading to cell- Ho mediated cytotoxicity. It is a statement of the present the present of the present the present of the present the present of the presen					do bind antigen. NK cells	example, hyperplasia,
killing of turnor cells and also Precognize antibody bound on target cells, via NK Fc Feepptors, leading to cell-Promediated cytotoxicity.  Inediated cytotoxicity.  Indiated					show antibody-independent	metaplasia, and/or dysplasia.
recognize antibody bound on and target cells, via NK Fc receptors, leading to cell- HO mediated cytotoxicity. Pla mediated cytotoxicity. Pla my art dis dis dis lead to the cell- HOTEN81 1085 CD152 in Human T cells cells ast hDTEN81 1086 Assays for the activation of Assays for the activation of the cell state of the c					killing of tumor cells and also	Preferred indications include
target cells, via NK Fc leu receptors, leading to cell- Ho mediated cytotoxicity. Pla my art diss diss leading to cell- lym art diss leading to cell- lym art diss leading to cell- lym art diss leading loss cells leading to cell- loss leading loss cells large leading loss cells loss distribution of Assays for the activation of leading leading leading leading leading leading leading loss leading l					recognize antibody bound on	anemia, pancytopenia,
HDTEN81 1085 CD152 in Human T Heceptors, leading to cell- lyn mediated cytotoxicity. Pla mediated cyto					target cells, via NK Fc	leukopenia, thrombocytopenia,
mediated cytotoxicity.   lyn					receptors, leading to cell-	Hodgkin's disease, acute
Pla my art dis					mediated cytotoxicity.	lymphocytic anemia (ALL),
HDTEN81   1085   Activation of   Assays for the activation of   Harten   HDTEN   HOTTEN   H						plasmacytomas, multiple
Activation of HDTE17   1086   Activation of Head activation of Head are a single of the activation of t						myeloma, Burkitt's lymphoma,
HDTEN81   1085   Activation of   Assays for the activation of   Colstant						arthritis, AIDS, granulomatous
HDTE17   1086   Activation of   Assays for the activation of   Horestands   Hores						disease, inflammatory bowel
HDTE17   1086   Activation of   Assays for the activation of   Public   P						disease, sepsis, neutropenia,
HDTEN81   1085   Activation of Horest   Assays for the activation of HDTE17   1086   Activation of Horest   Assays for the activation of Horest   1086   A						neutrophilia, psoriasis,
HDTEN81   1085   Activation of HDTE17   1086   Activation of HDTE17   Ac						suppression of immune
HDTEN81   1085   CD152 in Human T   ast cells   Assays for the activation of						reactions to transplanted
HDTEN81   1085   CD152 in Human T   ast   cells   Assays for the activation of   CD152 in Human T   CO152						organs and tissues,
HDTEN81   1085   CD152 in Human T   ast   cells   Assays for the activation of   Assays for the activation of						hemophilia, hypercoagulation,
HDTEN81   1085   CD152 in Human T   ast cells   Assays for the activation of   Assays for the activation of						diabetes mellitus, endocarditis,
HDTEN81   1085   CD152 in Human T   cells   Assays for the activation of   Assays for the activation of				-		meningitis, Lyme Disease,
HDTEN81 1085 CD152 in Human T cells Assays for the activation of						asthma and allergy.
HDTFE17 1086 Activation of Assays for the activation of	137	HDTEN81	1085	CD152 in Human T cells		
		HDTFE17	1086	Activation of	Assays for the activation of	Highly preferred indications

																									—
include blood disorders (e.g., as described below under "Immune Activity", "Blood-	"Cardiovascular Disorders"). Hiohly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	multiple sclerosis and/or as	described below),	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune	response, and suppressing a T	cell-mediated immune	response. Additional highly	preferred indications include	inflammation and	inflammatory disorders. An	additional highly preferred	indication is infection (e.g., an	infectious disease as described	, H		indications include neoplastic	diseases (e.g., leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred
transcription through the Nuclear Factor of Activated T cells (NFAT) response element	are well-known in the art and may be used or routinely modified to assess the ability	of polypeptides of the	invention (including antibodies	the invention) to regulate	NFAT transcription factors and	modulate expression of genes	involved in	immunomodulatory functions.	Exemplary assays for	transcription through the	NFAT response element that	may be used or routinely	modified to test NFAT-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Aramburu et al., J Exp Med
through NFAT response element in	immune cens (such as natural killer	.(2003)																-							
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138																		-							

			182(3):801-810 (1995); De	indications include neoplasms
			Boer et al., Int J Biochem Cell	and cancers, such as, for
			Biol 31(10):1221-1236 (1999);	example, leukemia, lymphoma,
			Fraser et al., Eur J Immunol	and prostate, breast, lung,
			29(3):838-844 (1999); and	colon, pancreatic, esophageal,
			Yeseen et al., J Biol Chem	stomach, brain, liver and
			268(19):14285-14293 (1993),	urinary cancer. Other preferred
			the contents of each of which	indications include benign
			are herein incorporated by	dysproliferative disorders and
			reference in its entirety. NK	pre-neoplastic conditions, such
			cells that may be used	as, for example, hyperplasia,
			according to these assays are	metaplasia, and/or dysplasia.
			publicly available (e.g.,	Preferred indications also
			through the ATCC).	include anemia, pancytopenia,
			Exemplary human NK cells	leukopenia, thrombocytopenia,
	···		that may be used according to	Hodgkin's disease, acute
			these assays include the NK-	lymphocytic anemia (ALL),
			YT cell line, which is a human	plasmacytomas, multiple
			natural killer cell line with	myeloma, Burkitt's lymphoma,
			cytolytic and cytotoxic	arthritis, AIDS, granulomatous
	·		activity.	disease, inflammatory bowel
				disease, sepsis, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, Lyme Disease,
				asthma and allergy.
HDTGC73	1087	Production of	Assays for measuring	Preferred embodiments of the

139			ICAM-1	expression of ICAM-1 are	invention include using
\ \ \				well-known in the art and may	polypeptides of the invention
				be used or routinely modified	(or antibodies, agonists, or
				to assess the ability of	antagonists thereof) in
				polypeptides of the invention	detection, diagnosis,
				including antibodies and	prevention, and/or treatment of
				agonists or antagonists of the	Inflammation, Vascular
				invention) to regulate ICAM-1	Disease, Athereosclerosis,
			)	expression. Exemplary assays	Restenosis, and Stroke
				that may be used or routinely	
				modified to measure ICAM-1	
				expression include assays	
				disclosed in: Takacs P, et al,	
				FASEB J, 15(2):279-281	-
				(2001); and, Miyamoto K, et	
				al., Am J Pathol, 156(5):1733-	
				1739 (2000), the contents of	
				each of which is herein	
				incorporated by reference in its	
				entirety. Cells that may be	
				used according to these assays	
				are publicly available (e.g.,	
				through the ATCC) and/or	
			,	may be routinely generated.	
				Exemplary cells that may be	
				used according to these assays	
	-			include microvascular	
				endothelial cells (MVEC).	
	HDTIT10	1088	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
140				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for

stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g.,	reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement	of mucosal immunity. Highly preferred indications include blood disorders (e.g., as	"Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"),	and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include	autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting a B cellmediated immune response and alternatively suppressing a B cell-mediated immune
participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces evtotoxic T cells.	Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas,	myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory	proteins produced by a large variety of cells where the expression level is strongly	regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to	assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate	immunomodulation and differentiation and modulate T cell proliferation and function. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-6, and
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response. Highly preferred indications include inflammation and inflammatory	disorders. Additional highly preferred indications include asthma and allergy. Highly preferred indications include	neoplastic diseases (e.g., myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and/or as described	below under "Hyperproliferative Disorders"). Highly preferred	indications include neoplasms and cancers, such as, myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and	prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred	indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia,	metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia,
the stimulation and upregulation of T cell proliferation and functional activities. Such assays that	may be used or routinely modified to test immunomodulatory and differentiation activity of	polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays	disclosed in Miraglia et al., J Biomolecular Screening 4:193- 204(1999); Rowland et al.,	"Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925	(1997), the contents of each of which are herein incorporated by reference in its entirety.  Human dendritic cells that may	be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art.	Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen

				and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
					granulomatous disease, inflammatory bowel disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
,					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					meningitis and I vme Disease
					An additional preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
	HDTIT10	1088	SEAP in		
140	· ·		HepG2/Squale-		
			synthetase(stimulati on)		
	HDTMK50	1089	Activation of	Kinase assay. Kinase assays,	A highly preferred
141			Natural Killer Cell	for example an Elk-1 kinase	embodiment of the invention
			ERK Signaling	assay, for ERK signal	includes a method for
			Pathway.	transduction that regulate cell	stimulating natural killer cell
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment
				may be used or routinely	of the invention includes a
				modified to assess the ability	method for inhibiting natural

8	ation. K See	and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101 (1998); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479- "Immune Activity" and described below under "Hyperproliferative Disorders", blood disorders (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity"), and (1999); Chang and Karin, Prog (e.g., as described below under "Immune disorders"), immune disorders (e.g., as described below under "Immune Activity", and/or "Blood-Related "Immune disorders"), immune disorders (e.g., as described below under "Immune disorders"), immune disorders (e.g., as described below under "Immune disorders"), immune disorders (e.g., as described below under "Immune disorders"), immune disorders (e.g., as described below under "Immune disorders"), immune disorders (e.g., as described below under "Immune disorders"), immune disorders (e.g., as described below under "Immune disorders"), immune disorders (e.g., as described below under "Immune disorders"), immune disorders (e.g., as described below under "Immune disorders"), immune disorders (e.g., as described below under "Immune disorders"), immune disorders (e.g., as described below under "Immune disorders"), immune disorders (e.g., as described below under "Immune disorders"), immune disorders (e.g., as described below under "Immune disorders"), immune disorders (e.g., as described below under "Immune disorders"), immune disorders (e.g., as described bel	

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Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis,	systemic lupus erythematosis, multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Highly preferred indications	also include cancers such as,	kidney, melanoma, prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver, urinary cancer,	lymphoma and leukemias.	Other preferred indications	include benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Other highly preferred	indications include,	pancytopenia, leukopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), arthritis, asthma,	AIDS, granulomatous disease,
according to these assays include the human natural killer cell lines (for example,	NK-YT cells which have cytolytic and cytotoxic	activity) or primary NK cells.		- Ar																		## 1 - iP					
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					inflammatory howel disease
_					sepsis, psoriasis, immine
					reactions to transplanted
					organs and tissues,
					endocarditis, meningitis, Lyme
				The state of the s	Disease, and allergies.
	HE2DY70	1090	Production of	IFNgamma FMAT. IFNg plays	A highly preferred
142			IFNgamma using a	a central role in the immune	embodiment of the invention
			T cells	system and is considered to be	includes a method for
				a proinflammatory cytokine.	stimulating the production of
				IFNg promotes TH1 and	IFNg. An alternative highly
				inhibits TH2 differentiation;	preferred embodiment of the
				promotes IgG2a and inhibits	invention includes a method
				IgE secretion; induces	for inhibiting the production of
				macrophage activation; and	IFNg. Highly preferred
				increases MHC expression.	ons
				Assays for immunomodulatory	disorders (e.g., as described
				proteins produced by T cells	below under "Immune
				and NK cells that regulate a	Activity", "Blood-Related
				variety of inflammatory	Disorders", and/or
				activities and inhibit TH2	"Cardiovascular Disorders"),
				helper cell functions are well	and infection (e.g., viral
				known in the art and may be	infections, tuberculosis,
				used or routinely modified to	infections associated with
				assess the ability of	chronic granulomatosus
				polypeptides of the invention	disease and malignant
				(including antibodies and	osteoporosis, and/or as
				agonists or antagonists of the	described below under
				invention) to mediate	"Infectious Disease"). Highly
				immunomodulation, regulate	preferred indications include
	79877			inflammatory activities,	autoimmune disease (e.g.,

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modulate TH2 helper cell function, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as Interferon gamma (IFNg), and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Ann Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the	modulate TH2 helper cell function, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunity evaluate the production of cytokines, such as Interferon gamma (IFNg), and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" (Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Ann NY Acad Sci 856:22-32 (1998); Behm et al., Ann Nev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the	rheumatoid arthritis, systemic lupus erythematosis, multiple	scierosis and/or as described below), immunodeficiency	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Additional preferred	indications include idiopathic	pulmonary fibrosis. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	Lonian discondificanting
		modulate TH2 helper cell function, and/or mediate	humoral or cell-mediated immunity. Exemplary assays	that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as Interferon	gamma (IFNg), and the	activation of T cells. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Gonzalez et al., J Clin	Lab Anal 8(5):225-233 (1995);	Billiau et al., Ann NY Acad	Sci 856:22-32 (1998); Boehm	et al., Annu Rev Immunol	15:749-795 (1997), and	Rheumatology (Oxford)	38(3):214-20 (1999), the	and deiding of and to high and

				herein incorporated by	disorders and pre-neoplastic
				reference in its entirety.	conditions, such as, for
				Human T cells that may be	example, hyperplasia,
				used according to these assays	metaplasia, and/or dysplasia.
				may be isolated using	Preferred indications include
				techniques disclosed herein or	anemia, pancytopenia,
				otherwise known in the art.	leukopenia, thrombocytopenia,
				Human T cells are primary	Hodgkin's disease, acute
				human lymphocytes that	lymphocytic anemia (ALL),
				mature in the thymus and	plasmacytomas, multiple
				express a T Cell receptor and	myeloma, Burkitt's lymphoma,
				CD3, CD4, or CD8. These	arthritis, AIDS, granulomatous
				cells mediate humoral or cell-	disease, inflammatory bowel
	·- ·-			mediated immunity and may	disease, sepsis, neutropenia,
				be preactivated to enhance	neutrophilia, psoriasis,
				responsiveness to	suppression of immune
				immunomodulatory factors.	reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
,	HE2EB74	1091	Activation of	Kinase assay. JNK and p38	A highly preferred
143			Endothelial Cell	kinase assays for signal	embodiment of the invention
			p38 or JNK	transduction that regulate cell	includes a method for
			Signaling Pathway.	proliferation, activation, or	stimulating endothelial cell
				apoptosis are well known in	growth. An alternative highly
				the art and may be used or	preferred embodiment of the
				routinely modified to assess	invention includes a method
				the ability of polypeptides of	for inhibiting endothelial cell
				the invention (including	growth. A highly preferred

	antibodies and agonists or	embodiment of the invention
	antagonists of the invention) to	includes a method for
	promote or inhibit cell	stimulating endothelial cell
	proliferation, activation, and	proliferation. An alternative
	apoptosis. Exemplary assays	highly preferred embodiment
	for JNK and p38 kinase	of the invention includes a
	activity that may be used or	method for inhibiting
	routinely modified to test JNK	endothelial cell proliferation.
	and p38 kinase-induced	A highly preferred
	activity of polypeptides of the	embodiment of the invention
	invention (including antibodies	includes a method for
	and agonists or antagonists of	stimulating apoptosis of
	the invention) include the	endothelial cells. An
	assays disclosed in Forrer et	alternative highly preferred
-	al., Biol Chem 379(8-9):1101-	embodiment of the invention
	1110 (1998); Gupta et al., Exp	includes a method for
	Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
	(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
	Soc Symp 64:29-48 (1999);	A highly preferred
	Chang and Karin, Nature	embodiment of the invention
	410(6824):37-40 (2001); and	includes a method for
	Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
	the contents of each of which	alternative highly preferred
	are herein incorporated by	embodiment of the invention
	reference in its entirety.	includes a method for
	Endothelial cells that may be	inhibiting (e.g., decreasing) the
	used according to these assays	activation of and/or
	are publicly available (e.g.,	inactivating endothelial cells.
	through the ATCC).	A highly preferred
	Exemplary endothelial cells	embodiment of the invention

includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial infarction chronic
that may be used according to	these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line	venous blood vessels, and are	involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.												-							
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hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis.
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hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,
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and cancer. Highly preferred indications also include trauma such as	wounds, burns, and injured tissue (e.g., vascular injury	such as, injury resulting from balloon angioplasty, and	atheroschlerotic lesions), implant fixation. scarring	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	D C

					blood disorders (e.g., as
					described below under
					"Immune Activity", "Blood-
					Related Disorders", and/or
•					"Cardiovascular Disorders").
					Preferred indications include
					autoimmune diseases (e.g.,
					rheumatoid arthritis, systemic
					lupus erythematosis, multiple
					sclerosis and/or as described
					below) and
					immunodeficiencies (e.g., as
					described below). Additional
					preferred indications include
					inflammation and
<u> </u>					inflammatory disorders (such
					as acute and chronic
					inflammatory diseases, e.g.,
		-			inflammatory bowel disease
**					and Crohn's disease), and pain
					management.
H_	HE2EN04	1092	Activation of JNK	Kinase assay. JNK kinase	Highly preferred indications
			Signaling Pathway	assays for signal transduction	include asthma, allergy,
			in immune cells	that regulate cell proliferation,	hypersensitivity reactions,
			(such as	activation, or apoptosis are	inflammation, and
			eosinophils).	well known in the art and may	inflammatory disorders.
				be used or routinely modified	Additional highly preferred
				to assess the ability of	indications include immune
				polypeptides of the invention	and hematopoietic disorders
		\		(including antibodies and	(e.g., as described below under
				agonists or antagonists of the	"Immine Activity" and

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"Rlood-Related Disorders")	autoimmine diseases (e a	rheumatoid arthritic exetemic	limis erythematosis Crohn's	disease, multiple sclerosis	and/or as described below).	immunodeficiencies (e.g., as	described below). Highly	preferred indications also	include boosting or inhibiting	immune cell proliferation.	Preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as	described below under	"Hyperproliferative	Disorders"). Highly preferred	indications include boosting an	eosinophil-mediated immune	response, and suppressing an	eosinophil-mediated immune	response.									
invention) to promote or	inhibit cell proliferation	activation, and anontosis	Exemplary assays for INK	kinase activity that may be	used or routinely modified to	test JNK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Gupta et al., Exp	Cell Res 247(2): 495-504	(1999); Kyriakis JM, Biochem	Soc Symp 64:29-48 (1999);	Chang and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Exemplary cells that may be	used according to these assays	include eosinophils.	Eosinophils are important in	the late stage of allergic	reactions; they are recruited to	ticenee and mediate the
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		-																												

inflammatory response of late stage allergic reaction.  Moreover, exemplary assays that may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate signal transduction, cell proliferation, activation, or apoptosis in eosinophilis include assays disclosed and/or cited in: Zhang IP, et al., "Role of caspases in dexamethasone-induced apoptosis and activation of e-Jun NH2-terminal kinase and p38 mitogen-activated protein kinase in human cosinophils."  Clin Exp Immunol; Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fax receptor signaling by nitric oxide in eosinophils' J Exp Med; Feb 2:187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Souga AR, et al.," In vivo																																
	. 13	inflammatory response of late	stage allergic reaction.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and	activation of c-Jun NH2-	terminal kinase and p38	mitogen-activated protein	kinase in human eosinophils"	Clin Exp Immunol;	Oct;122(1):20-7 (2000);	Hebestreit H, et al.,	"Disruption of fas receptor	signaling by nitric oxide in	eosinophils" J Exp Med; Feb	2;187(3):415-25 (1998); J	Allergy Clin Immunol 1999	Sep;104(3 Pt 1):565-74; and,	Sousa AR, et al., "In vivo	resistance to corticosteroids in
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	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Vascular Disease, Atherosclerosis, Restenosis, Stroke, and Asthma.
bronchial asthma is associated with enhanced phosyphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Rolfe BE, et al., Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365 (1995); and, Grunstein MM, et al., Am J Physiol Lung Cell
	Production of ICAM-1
	1093
	HE2FV03
	145

		Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders", blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders", and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include	autoimmune diseases (e.g.,
Mol Physiol, 278(6):L1154-L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include Aortic Smooth Muscle Cells (AOSMC); such as bovine AOSMC.		Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit immune cell (e.g. T-cell) proliferation, activation, and apoptosis.	exemplary assays for JINK and
	SEAP in OE-33	Activation of T-Cell p38 or JNK Signaling Pathway.	the state of the s
	1093	1094	
	HE2FV03	HE2NV57	
	145	146	

p38 kinase activity that may be	rheumatoid arthritis, systemic
_	lupus erythematosis, multiple
test JNK and p38 kinase-	sclerosis and/or as described
induced activity of	below) and
polypeptides of the invention	immunodeficiencies (e.g., as
(including antibodies and	described below). Additional
agonists or antagonists of the	highly preferred indications
invention) include the assays	include inflammation and
disclosed in Forrer et al., Biol	inflammatory disorders.
Chem 379(8-9):1101-1110	Highly preferred indications
(1998); Gupta et al., Exp Cell	also include neoplastic
Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
Kyriakis JM, Biochem Soc	lymphoma, and/or as described
Symp 64:29-48 (1999); Chang	below under
and Karin, Nature	"Hyperproliferative
410(6824):37-40 (2001); and	Disorders"). Highly preferred
Cobb MH, Prog Biophys Mol	indications include neoplasms
Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
the contents of each of which	lymphoma, prostate, breast,
are herein incorporated by	lung, colon, pancreatic,
reference in its entirety. T	esophageal, stomach, brain,
cells that may be used	liver, and urinary cancer. Other
according to these assays are	preferred indications include
publicly available (e.g.,	benign dysproliferative
through the ATCC).	disorders and pre-neoplastic
Exemplary mouse T cells that	conditions, such as, for
may be used according to these	example, hyperplasia,
assays include the CTLL cell	metaplasia, and/or dysplasia.
line, which is an IL-2	Preferred indications include
dependent suspension-culture	arthritis, asthma, AIDS,
cell line with cytotoxic	allergy, anemia, pancytopenia,

HE2NV57 1094 Insulin Secretion Assays		lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.
	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key	A highly preferred indication is diabetes mellitus. An additional highly preferred indication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic

	Exemplary assays that may be	blockage). seizures, mental
	used or routinely modified to	confusion, drowsiness,
	test for stimulation of insulin	nonketotic hyperglycemic-
	secretion (from pancreatic	hyperosmolar coma,
	cells) by polypeptides of the	cardiovascular disease (e.g.,
	invention (including antibodies	heart disease, atherosclerosis,
	and agonists or antagonists of	microvascular disease,
1.1.	the invention) include assays	hypertension, stroke, and other
	disclosed in: Shimizu, H., et	diseases and disorders as
	al., Endocr J, 47(3):261-9	described in the
	(2000); Salapatek, A.M., et al.,	"Cardiovascular Disorders"
	Mol Endocrinol, 13(8):1305-	section below), dyslipidemia,
	17 (1999); Filipsson, K., et al.,	endocrine disorders (as
	Ann N Y Acad Sci, 865:441-4	described in the "Endocrine
	(1998); Olson, L.K., et al., J	Disorders" section below),
	Biol Chem, 271(28):16544-52	neuropathy, vision impairment
	(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and
	Journal of Biomolecular	blindness), ulcers and impaired
	Screening, 4:193-204 (1999),	wound healing, and infection
	the contents of each of which	(e.g., infectious diseases and
	is herein incorporated by	disorders as described in the
	reference in its entirety.	"Infectious Diseases" section
	Pancreatic cells that may be	below, especially of the
	used according to these assays	urinary tract and skin), carpal
	are publicly available (e.g.,	tunnel syndrome and
	through the ATCC) and/or	Dupuytren's contracture).
	may be routinely generated.	An additional highly preferred
	Exemplary pancreatic cells that	indication is obesity and/or
	may be used according to these	complications associated with
	assays include HITT15 Cells.	obesity. Additional highly
	HITT15 are an adherent	preferred indications include

				epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78:	weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.
146	HE2NV57	1094	TNFa in Human T-cell 293T	4339-4343, 1981.	
147	НЕ2РD49	1095	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6	A highly preferred embodiment of the invention includes a method for
				participates in IL-4 induced IgE production and increases IgA production (IgA plays a	stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment
				role in mucosal immunity). IL-6 induces cytotoxic T cells.	of the invention includes a method for inhibiting (e.g.,
				Deregulated expression of IL-6 has been linked to autoimmune	reducing) IL-6 production. A highly preferred indication is
				disease, plasmacytomas, myelomas, and chronic hynermroliferative diseases	the stimulation or enhancement of mucosal immunity. Highly preferred indications include

		Assavs for immunomodulatory	blood disorders (e.g. as
		and differentiation factor	described below under
		proteins produced by a large	"Immune Activity", "Blood-
		variety of cells where the	Related Disorders", and/or
		expression level is strongly	"Cardiovascular Disorders"),
		regulated by cytokines, growth	and infection (e.g., as
		factors, and hormones are well	described below under
		known in the art and may be	"Infectious Disease"). Highly
		used or routinely modified to	preferred indications include
		assess the ability of	autoimmune diseases (e.g.,
		polypeptides of the invention	rheumatoid arthritis, systemic
-	- "	(including antibodies and	lupus erythematosis, multiple
		agonists or antagonists of the	sclerosis and/or as described
		invention) to mediate	below) and
		immunomodulation and	immunodeficiencies (e.g., as
		differentiation and modulate T	described below). Highly
		cell proliferation and function.	preferred indications also
		Exemplary assays that test for	include boosting a B cell-
		immunomodulatory proteins	mediated immune response
		evaluate the production of	and alternatively suppressing a
		cytokines, such as IL-6, and	B cell-mediated immune
		the stimulation and	response. Highly preferred
		upregulation of T cell	indications include
		proliferation and functional	inflammation and
		activities. Such assays that	inflammatory
		may be used or routinely	disorders. Additional highly
		modified to test	preferred indications include
		immunomodulatory and	asthma and allergy. Highly
		diffferentiation activity of	preferred indications include
		polypeptides of the invention	neoplastic diseases (e.g.,
		(including antibodies and	myeloma, plasmacytoma,

		agonists or antagonists of the	leukemia, lymphoma,
		invention) include assays	melanoma, and/or as described
		disclosed in Miraglia et al., J	below under
		Biomolecular Screening 4:193-	"Hyperproliferative
		204(1999); Rowland et al.,	Disorders"). Highly preferred
	• **	"Lymphocytes: a practical	indications include neoplasms
		approach" Chapter 6:138-160	and cancers, such as, myeloma,
		(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
		Immunol 158:2919-2925	lymphoma, melanoma, and
		(1997), the contents of each of	prostate, breast, lung, colon,
		which are herein incorporated	pancreatic, esophageal,
		by reference in its entirety.	stomach, brain, liver and
		Human dendritic cells that may	urinary cancer. Other preferred
		be used according to these	indications include benign
	•	assays may be isolated using	dysproliferative disorders and
		techniques disclosed herein or	pre-neoplastic conditions, such
		otherwise known in the art.	as, for example, hyperplasia,
		Human dendritic cells are	metaplasia, and/or dysplasia.
		antigen presenting cells in	Preferred indications include
		suspension culture, which,	anemia, pancytopenia,
		when activated by antigen	leukopenia, thrombocytopenia,
4.31		and/or cytokines, initiate and	Hodgkin's disease, acute
		upregulate T cell proliferation	lymphocytic anemia (ALL),
		and functional activities.	multiple myeloma, Burkitt's
			lymphoma, arthritis, AIDS,
-			granulomatous disease,
			inflammatory bowel disease,
			sepsis, neutropenia,
			neutrophilia, psoriasis,
			suppression of immune
			reactions to transplanted

organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").				Reporter Assay: construct	contains regulatory and coding	sequence of squalene	synthetase, the first specific	enzyme in the cholesterol	biosynthetic pathway. See	Jiang, et al., J. Biol. Chem.	268:12818-128241(993), the	contents of which are herein	incorporated by reference in its	entirety. Cells were treated	with SID supernatants, and	SEAP activity was measured	after 72 hours. HepG2 is a	human hepatocellular	Oscinoms cell line (ATC)
				Repor	contai	sedner	synthe	enzym	biosyn	Jiang,	268:12	conter	incorp	entiret	with S	SEAP	after 7	humar	carcin
	IL-2 in Human T-cell 2B9	CD152 in Human T cells	SEAP in Jurkat/IL4 promoter	Inhibition of	squalene synthetase	gene transcription.													
	1095	1096	1096	1097															
	НЕ2РD49	HE2PY40	HE2PY40	HE6EU50								-							
	147	148	148		149														

-				HB-8065). See Knowles et al., Science 200-407-9 (1980). the	
				contents of which are herein	
				incorporated by reference in its entirety.	
149	HE6EU50	1097	CD69 in Human T		
149	HE6EU50	1097	IL-2 in Human T-cell 293T		
	HE6EU50	1097	Activation of	Assays for the activation of	Highly preferred indications
149			transcription	transcription through the	include blood disorders (e.g.,
			through NFAT	Nuclear Factor of Activated T	as described below under
			response in immune	cells (NFAT) response element	"Immune Activity", "Blood-
			cells (such as T-	are well-known in the art and	Related Disorders", and/or
			cells).	may be used or routinely	"Cardiovascular Disorders").
				modified to assess the ability	Highly preferred indications
				of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
				and agonists or antagonists of	systemic lupus erythematosis,
				the invention) to regulate	multiple sclerosis and/or as
				NFAT transcription factors and	described below),
				modulate expression of genes	immunodeficiencies (e.g., as
				involved in	described below), boosting a T
				immunomodulatory functions.	cell-mediated immune
				Exemplary assays for	response, and suppressing a T
				transcription through the	cell-mediated immune
				NFAT response element that	response. Additional highly
				may be used or routinely	preferred indications include
				modified to test NFAT-	inflammation and
				response element activity of	inflammatory disorders. An
				polypeptides of the invention	additional highly preferred

	(including antibodies and	indication is infection (e.g., an
	agonists or antagonists of the	infectious disease as described
	invention) include assays	below under "Infectious
	disclosed in Berger et al., Gene	Disease"). Preferred
	66:1-10 (1998); Cullen and	indications include neoplastic
	Malm, Methods in Enzymol	diseases (e.g., leukemia,
	216:362-368 (1992); Henthorn	lymphoma, and/or as described
	et al., Proc Natl Acad Sci USA	below under
	85:6342-6346 (1988); Serfling	"Hyperproliferative
	et al., Biochim Biophys Acta	Disorders"). Preferred
	1498(1):1-18 (2000); De Boer	indications include neoplasms
	et al., Int J Biochem Cell Biol	and cancers, such as, for
	31(10):1221-1236 (1999);	example, leukemia, lymphoma,
	Fraser et al., Eur J Immunol	and prostate, breast, lung,
	29(3):838-844 (1999); and	colon, pancreatic, esophageal,
	Yeseen et al., J Biol Chem	stomach, brain, liver and
	268(19):14285-14293 (1993),	urinary cancer. Other preferred
	the contents of each of which	indications include benign
	are herein incorporated by	dysproliferative disorders and
	reference in its entirety. T	pre-neoplastic conditions, such
	cells that may be used	as, for example, hyperplasia,
	according to these assays are	metaplasia, and/or dysplasia.
	publicly available (e.g.,	Preferred indications also
	through the ATCC).	include anemia, pancytopenia,
	Exemplary human T cells that	leukopenia, thrombocytopenia,
	may be used according to these	Hodgkin's disease, acute
	assays include the JURKAT	lymphocytic anemia (ALL),
	cell line, which is a suspension	plasmacytomas, multiple
	culture of leukemia cells that	myeloma, Burkitt's lymphoma,
	produce IL-2 when stimulated.	arthritis, AIDS, granulomatous
		disease, inflammatory bowel

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conditions, such as, for example, hyperplasia.	metaplasia, and/or dysplasia.	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an	infectious disease as described	helow under "Infections
of polypeptides of the invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary human T cells,	such as the MOLT4 cell line,	that may be used according to	these assays are publicly	available (e.g., through the	ATCC).								
															-														
																***		-							75 12				
												-	_															-	

					Disease"). An additional
					preferred indication is
					idiopathic pulmonary fibrosis.
_					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					acute lymphocytic anemia
					(ALL), plasmacytomas,
					multiple myeloma, arthritis,
					AIDS, granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
_					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, and
					asthma and allergy.
•	HE8DS15	1098	Activation of	Kinase assay. Kinase assays,	A highly preferred
_			Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
			Signaling Pathway	assay, for ERK signal	includes a method for
				transduction that regulate cell	stimulating adipocyte
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment
				may be used or routinely	of the invention includes a
				modified to assess the ability	method for inhibiting
				of polypeptides of the	adipocyte proliferation. A
				invention (including antibodies	highly preferred embodiment
				and agonists or antagonists of	of the invention includes a

the invention) to promote or	method for stimulating
 inhibit cell proliferation,	adipocyte differentiation. An
activation, and differentiation.	alternative highly preferred
Exemplary assays for ERK	embodiment of the invention
kinase activity that may be	includes a method for
used or routinely modified to	inhibiting adipocyte
test ERK kinase-induced	differentiation. A highly
activity of polypeptides of the	preferred embodiment of the
invention (including antibodies	invention includes a method
and agonists or antagonists of	for stimulating (e.g.,
the invention) include the	increasing) adipocyte
 assays disclosed in Forrer et	activation. An alternative
al., Biol Chem 379(8-9):1101-	highly preferred embodiment
1110 (1998); Le Marchand-	of the invention includes a
Brustel Y, Exp Clin	method for inhibiting the
Endocrinol Diabetes	activation of (e.g., decreasing)
 107(2):126-132 (1999);	and/or inactivating adipocytes.
 Kyriakis JM, Biochem Soc	Highly preferred indications
Symp 64:29-48 (1999); Chang	include endocrine disorders
and Karin, Nature	(e.g., as described below under
410(6824):37-40 (2001); and	"Endocrine Disorders").
Cobb MH, Prog Biophys Mol	Highly preferred indications
Biol 71(3-4):479-500 (1999);	also include neoplastic
the contents of each of which	diseases (e.g., lipomas,
are herein incorporated by	liposarcomas, and/or as
reference in its entirety.	described below under
Mouse adipocyte cells that	"Hyperproliferative
 may be used according to these	Disorders"). Preferred
assays are publicly available	indications include blood
. (e.g., through the ATCC).	disorders (e.g., hypertension,
Exemplary mouse adipocyte	congestive heart failure, blood

according to these assays include 373-11 cells. 373-1.  is an adherent mouse preadipocyte cell line that is a continuous substrain of 373 finetural problast cells developed through clonal isolation and through clonal isolation and undergo a pre-adipocyte to adipocyte to adipocy			cells that may be used	vessel blockage, heart disease,	
	-		according to these assays	stroke, impotence and/or as	
			include 3T3-L1 cells. 3T3-L1	described below under	
			is an adherent mouse	"Immune Activity",	
			preadipocyte cell line that is a	"Cardiovascular Disorders",	
			continuous substrain of 3T3	and/or "Blood-Related	
			fibroblast cells developed	Disorders"), immune disorders	
			through clonal isolation and	(e.g., as described below under	
<del></del>			undergo a pre-adipocyte to	"Immune Activity"), neural	
· · · · · · · · · · · · · · · · · · ·			adipose-like conversion under	disorders (e.g., as described	
			appropriate differentiation	below under "Neural Activity	
and infection (e.g., described below un "Infectious Diseasa A highly preferred is diabetes mellitus additional highly prindication is a compassociated with dia diabetic retinopath nephropathy, kidne (e.g., renal failure, nephropathy and/o diseases and disort described in the "R Disorders" section diabetic neuropathy disease and nerve (e.g., due to diabetic neuropathy), blood neuropathy), neuropathy), neuropathy), neuropathy), neuropathy), neuropathy), neuropathy),			conditions known in the art.	and Neurological Diseases"),	_
described below un "Infectious Disease A highly preferred is diabetes mellitus additional highly p indication is a com associated with dia diabetic retinopath nephropathy, kidne (e.g., renal failure, nephropathy and/o diseases and disore described in the "R Disorders" section diabetic neuropath disease and nerve o (e.g., due to diabet neuropathy), blood				and infection (e.g., as	
"Infectious Diseasa A highly preferred is diabetes mellitus additional highly prindication is a com associated with dia diabetic retinopath nephropathy, kidne (e.g., renal failure, nephropathy and/o diseases and disord described in the "R Disorders" section diabetic neuropath disease and nerve (e.g., due to diabet neuropathy). blood				described below under	
A highly preferred is diabetes mellitus additional highly p indication is a com associated with dia diabetic retinopath nephropathy, kidne (e.g., renal failure, nephropathy and/o diseases and disord described in the "R Disorders" section diabetic neuropath disease and nerve (e.g., due to diabet neuropathy), blood				"Infectious Disease").	
is diabetes mellitus additional highly p indication is a com associated with dia diabetic retinopath nephropathy, kidns (e.g., renal failure, nephropathy and/o diseases and disord described in the "R Disorders" section diabetic neuropath disease and nerve ( e.g., due to diabet neuropathy), blood				A highly preferred indication	
additional highly p indication is a com associated with dia diabetic retinopath nephropathy, kidne (e.g., renal failure, nephropathy and/o diseases and disord described in the "R Disorders" section diabetic neuropath disease and nerve of (e.g., due to diabet neuropathy), blood				is diabetes mellitus. An	_
indication is a com associated with dia diabetic retinopath nephropathy, kidne (e.g., renal failure, nephropathy and/o diseases and disord described in the "R Disorders" section diabetic neuropath disease and nerve (e.g., due to diabet neuropathy), blood				additional highly preferred	
associated with dia diabetic retinopath nephropathy, kidne (e.g., renal failure, nephropathy and/o diseases and disord described in the "R Disorders" section diabetic neuropath disease and nerve (e.g., due to diabet neuropathy). blood		-		indication is a complication	
diabetic retinopath nephropathy, kidne (e.g., renal failure, nephropathy and/o diseases and disor described in the "R Disorders" section diabetic neuropath disease and nerve (e.g., due to diabet				associated with diabetes (e.g.,	
nephropathy, kidne (e.g., renal failure, nephropathy and/o diseases and disord described in the "R Disorders" section diabetic neuropathy disease and nerve (e.g., due to diabet neuropathy). blood neuropathy), blood				diabetic retinopathy, diabetic	_
(e.g., renal failure, nephropathy and/o diseases and disord described in the "R Disorders" section diabetic neuropathy disease and nerve (e.g., due to diabet neuropathy). blood neuropathy), blood				nephropathy, kidney disease	
nephropathy and/o diseases and disord described in the "R Disorders" section diabetic neuropath disease and nerve (e.g., due to diabet neuropathy). blood				(e.g., renal failure,	
diseases and disord described in the "R Disorders" section diabetic neuropath disease and nerve ( (e.g., due to diabet neuropathy). blood				nephropathy and/or other	
described in the "R Disorders" section diabetic neuropath disease and nerve (e.g., due to diabet neuropathy). blood				diseases and disorders as	
Disorders" section diabetic neuropath disease and nerve (e.g., due to diabet neuropathy). blood				described in the "Renal	
diabetic neuropath disease and nerve of (e.g., due to diabet				Disorders" section below),	
disease and nerve (e.g., due to diabet neuropathy). blood				diabetic neuropathy, nerve	
(e.g., due to diabet				disease and nerve damage	
neuropathy). blood				(e.g., due to diabetic	
				neuropathy), blood vessel	

blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly
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				_																			_							

preferred indications include weight loss or alternatively	weight loss of antendativery, weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. Preferred	indications include neoplasms	and cancer, such as,	Iymphoma, leukemia and	breast, colon, and kidney	cancer. Additional preferred	indications include melanoma,	prostate, lung, pancreatic,	esophageal, stomach, brain,	
					-																							-

					include linomas and
					liposarcomas. Other preferred
					indications include benign
	•				dysproliferative disorders and
					pre-neoplastic conditions, such
					as, for example, hyperplasia,
				10.000	metaplasia, and/or dysplasia.
	HE8DS15	1098	Regulation of	Assays for the regulation of	A highly preferred
150			transcription of	transcription of Malic Enzyme	indication is diabetes mellitus.
			Malic Enzyme in	are well-known in the art and	An additional highly preferred
			adipocytes	may be used or routinely	indication is a complication
				modified to assess the ability	associated with diabetes (e.g.,
				of polypeptides of the	diabetic retinopathy, diabetic
				invention (including antibodies	nephropathy, kidney disease
				and agonists or antagonists of	(e.g., renal failure,
				the invention) to regulate	nephropathy and/or other
				transcription of Malic Enzyme,	diseases and disorders as
				a key enzyme in lipogenesis.	described in the "Renal
				Malic enzyme is involved in	Disorders" section below),
				lipogenesisand its expression is	diabetic neuropathy, nerve
				stimulted by insulin. ME	disease and nerve damage
				promoter contains two direct	(e.g., due to diabetic
				repeat (DR1)- like elements	neuropathy), blood vessel
·				MEp and MEd identified as	blockage, heart disease, stroke,
				putative PPAR response	impotence (e.g., due to diabetic
-		•		elements. ME promoter may	neuropathy or blood vessel
				also responds to AP1 and other	blockage), seizures, mental
				transcription factors.	confusion, drowsiness,
				Exemplary assays that may be	nonketotic hyperglycemic-
				used or routinely modified to	hyperosmolar coma,
				test for regulation of	cardiovascular disease (e.g.,

transcription of Malic Enzyme	heart disease, atherosclerosis,
(in adipoocytes) by	microvascular disease,
 polypeptides of the invention	hypertension, stroke, and other
(including antibodies and	diseases and disorders as
agonists or antagonists of the	described in the
invention) include assays	"Cardiovascular Disorders"
disclosed in: Streeper, R.S., et	section below), dyslipidemia,
al., Mol Endocrinol,	endocrine disorders (as
12(11):1778-91 (1998);	described in the "Endocrine
Garcia-Jimenez, C., et al., Mol	Disorders" section below),
Endocrinol, 8(10):1361-9	neuropathy, vision impairment
(1994); Barroso, I., et al., J	(e.g., diabetic retinopathy and
Biol Chem, 274(25):17997-	blindness), ulcers and impaired
8004 (1999); Ijpenberg, A., et	wound healing, and infection
al., J Biol Chem,	(e.g., infectious diseases and
272(32):20108-20117 (1997);	disorders as described in the
Berger, et al., Gene 66:1-10	"Infectious Diseases" section
(1988); and, Cullen, B., et al.,	below, especially of the
Methods in Enzymol.	urinary tract and skin), carpal
216:362–368 (1992), the	tunnel syndrome and
contents of each of which is	Dupuytren's contracture).
herein incorporated by	An additional highly preferred
reference in its entirety.	indication is obesity and/or
Hepatocytes that may be used	complications associated with
according to these assays are	obesity. Additional highly
publicly available (e.g.,	preferred indications include
through the ATCC) and/or	weight loss or alternatively,
may be routinely generated.	weight gain. Aditional
Exemplary hepatocytes that	highly preferred indications are
may be used according to these	complications associated with
assays includes the H4IIE rat	insulin resistance.

				liver hepatoma cell line.	
	HE8DS15	1098	Inhibition of	Reporter Assay: construct	
150			squalene synthetase	contains regulatory and coding	
			gene transcription.	sequence of squalene	
				synthetase, the first specific	
				enzyme in the cholesterol	
				biosynthetic pathway. See	
				Jiang, et al., J. Biol. Chem.	
				268:12818-128241(993), the	
				contents of which are herein	
				incorporated by reference in its	
				entirety. Cells were treated	
				with SID supernatants, and	
				SEAP activity was measured	
				after 72 hours. HepG2 is a	
				human hepatocellular	
				carcinoma cell line (ATCC	
				HB-8065). See Knowles et al.,	
			-	Science. 209:497-9 (1980), the	
				contents of which are herein	
				incorporated by reference in its	
				entirety.	
	HE8MH91	1099	Activation of	Assays for the activation of	Preferred embodiments of the
151			transcription	transcription through the	invention include using
			through NFKB	NFKB response element are	polypeptides of the invention
			response element in	well-known in the art and may	(or antibodies, agonists, or
			immune cells (such	be used or routinely modified	antagonists thereof) in
			as B-cells).	to assess the ability of	detection, diagnosis,
				polypeptides of the invention	prevention, and/or treatment of
				(including antibodies and	Cancer, Autoimmunity,
				agonists or antagonists of the	Allergy and Asthma

invention) to regulate NFKB transcription factors and modulate expression of	Exemplary assays for transcription through the NFKB response element that	may be used or rountinely modified to test NFKB-response element activity of	(including antibodies and agonists or antagonists of the invention) include account	disclosed in: Gri G, et al., Biol Chem, 273(11):6431-6438	(2000); Berger et al., Gene 66:1-10 (1998); Cullen and	Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988): Valle	Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med	82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated

y. e used are that that cell							of highly preferred embodiment	<u>.</u>	I may   method for inhibiting (e.g.,	ified reducing) IL-4 production.	A highly preferred indication				indication includes rhinitis.	nulate   Additional highly preferred	indications include	, inflammation and	or inflammatory disorders.	Highly preferred indications	st for include neoplastic diseases
by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary immune cells that may be used according to these assays include the Reh B-cell line.		IL-4 FMAT. Assays for	immunomodulatory proteins	secreted by TH2 cells that	stimulate B cells, T cells,	macrophages and mast cells	and promote polarization of	CD4+ cells into TH2 cells are	well known in the art and may	be used or routinely modified	to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, stimulate	immune cells, modulate	immune cell polarization,	and/or mediate humoral or	cell-mediated immunity.	Exemplary assays that test for
	IgG in Human B cells SAC	Production of IL-4																			
	1100	1100														-			-		
	HE8QV67	HE8QV67																			
	152		152															-			

immunomodulatory proteins	(e.g., leukemia, lymphoma,
evaluate the production of	melanoma, and/or as described
cytokines, such as IL-4, and	below under
the stimulation of immune	"Hyperproliferative
cells, such as B cells, T cells,	Disorders"). Preferred
macrophages and mast cells.	indications include neoplasms
Such assays that may be used	and cancers, such as, for
or routinely modified to test	example, leukemia, lymphoma,
immunomodulatory activity of	melanoma, and prostate,
polypeptides of the invention	breast, lung, colon, pancreatic,
(including antibodies and	esophageal, stomach, brain,
agonists or antagonists of the	liver and urinary cancer. Other
invention) include the assays	preferred indications include
disclosed in Miraglia et al., J	benign dysproliferative
Biomolecular Screening 4:193-	disorders and pre-neoplastic
204 (1999); Rowland et al.,	conditions, such as, for
"Lymphocytes: a practical	example, hyperplasia,
approach" Chapter 6:138-160	metaplasia, and/or dysplasia.
(2000); Gonzalez et al., J Clin	Preferred indications include
Lab Anal 8(5):277-283 (1194);	blood disorders (e.g., as
Yssel et al., Res Immunol	described below under
144(8):610-616 (1993); Bagley	"Immune Activity", "Blood-
et al., Nat Immunol 1(3):257-	Related Disorders", and/or
261 (2000); and van der Graaff	"Cardiovascular Disorders").
et al., Rheumatology (Oxford)	Preferred indications include
38(3):214-220 (1999), the	autoimmune diseases (e.g.,
contents of each of which are	rheumatoid arthritis, systemic
herein incorporated by	lupus erythematosis, multiple
reference in its entirety.	sclerosis and/or as described
Human T cells that may be	below) and
used according to these assays	immunodeficiencies (e.g., as

				may be isolated using	described below). Preferred
				techniques disclosed herein or	a
				otherwise known in the art.	pancytopenia, leukopenia,
				Human T cells are primary	thrombocytopenia, Hodgkin's
				human lymphocytes that	disease, acute lymphocytic
				mature in the thymus and	anemia (ALL),
				express a T cell receptor and	plasmacytomas, multiple
				CD3, CD4, or CD8. These	myeloma, Burkitt's lymphoma,
				cells mediate humoral or cell-	arthritis, AIDS, granulomatous
				mediated immunity and may	disease, inflammatory bowel
				be preactivated to enhance	disease, sepsis, neutropenia,
				responsiveness to	neutrophilia, psoriasis,
				immunomodulatory factors.	suppression of immune
			,		reactions to transplanted
					organs and tissues,
	-				hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
,	HE9BK23	1101	IgG in Human B		
153			cells SAC		
	HE9BK23	1101	Activation of	Assays for the activation of	Highly preferred indications
153			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as T-cells).	to assess the ability of	as described below under

		polypeptides of the invention	"Immune Activity", "Blood-
		(including antibodies and	Related Disorders", and/or
-		agonists or antagonists of the	"Cardiovascular Disorders").
		invention) to regulate NFKB	Highly preferred indications
_		transcription factors and	include autoimmune diseases
		modulate expression of	(e.g., rheumatoid arthritis,
		immunomodulatory genes.	systemic lupus erythematosis,
		Exemplary assays for	multiple sclerosis and/or as
		transcription through the	described below), and
		NFKB response element that	immunodeficiencies (e.g., as
		may be used or rountinely	described below). An
		modified to test NFKB-	additional highly preferred
		response element activity of	indication is infection (e.g.,
		polypeptides of the invention	AIDS, and/or an infectious
		(including antibodies and	disease as described below
		agonists or antagonists of the	under "Infectious Disease").
*****		invention) include assays	Highly preferred indications
	- Authorities	disclosed in Berger et al., Gene	include neoplastic diseases
		66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
		Malm, Methods in Enzymol	lymphoma, and/or as described
		216:362-368 (1992); Henthorn	below under
		et al., Proc Natl Acad Sci USA	"Hyperproliferative
		85:6342-6346 (1988); Black et	Disorders"). Highly preferred
	ne re material	al., Virus Gnes 15(2):105-117	indications include neoplasms
		(1997); and Fraser et al.,	and cancers, such as, for
		29(3):838-844 (1999), the	example, melanoma, renal cell
		contents of each of which are	carcinoma, leukemia,
		herein incorporated by	lymphoma, and prostate,
		reference in its entirety.	breast, lung, colon, pancreatic,
-	- 2/144	Exemplary human T cells,	esophageal, stomach, brain,
		such as the MOLT4, that may	liver and urinary cancer. Other

preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia.	metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia,	leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL),	plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis. AIDS. granulomatous	disease, inflammatory bowel disease, sepsis, neutropenia.	neutrophilia, psoriasis,	hemophilia, hypercoagulation, diahetes mellitus endocarditis	meningitis, Lyme Disease,	suppression of immune	reactions to transplanted organs, asthma and allergy.	A highly preferred	embodiment of the invention	includes a method for	stimulating T cell proliferation.	An alternative highly preferred	embodiment of the invention	includes a method for	inhibiting T cell proliferation.
be used according to these assays are publicly available (e.g., through the ATCC).										Assays for the activation of	transcription through the CD28	response element are well-	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and
										Activation of	transcription	through CD28	response element in	immune cells (such	as T-cells).		
										1101		***					
			_							HE9BK23							
											153						

A highly preferred embodiment of the invention	includes a method for	activating T cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting the activation of	and/or inactivating T cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating (e.g., increasing)	IL-2 production. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting (e.g.,	reducing) IL-2 production.	Additional highly preferred	indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below),	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune
agonists or antagonists of the invention) to stimulate IL-2	expression in T cells.	Exemplary assays for	transcription through the CD28	response element that may be	used or routinely modified to	test CD28-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	McGuire and Iacobelli, J	Immunol 159(3):1319-1327	(1997); Parra et al., J Immunol	166(4):2437-2443 (2001); and	Butscher et al., J Biol Chem	(3(1):552-560 (1998), the	contents of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).
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response, and suppressing a T cell-mediated immune response. Highly preferred	indications include neoplastic diseases (e.g., melanoma, renal	cell carcinoma, leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, melanoma (e.g.,	metastatic melanoma), renal	cell carcinoma (e.g., metastatic	renal cell carcinoma),	leukemia, lymphoma (e.g., T	cell lymphoma), and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	A highly preferred indication	includes infection (e.g.,	AIDS, tuberculosis, infections	associated with granulomatous
Exemplary human T cells that may be used according to these assays include the SUPT cell	line, which is a suspension culture of IL-2 and IL-4	responsive T cells.						-							-									- Constant of the Constant of			
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disease, and osteoporosis,	and/or as described below	under "Infectious Disease"). A	highly preferred indication is	AIDS. Additional highly	preferred indications include	suppression of immune	reactions to transplanted	organs and/or tissues, uveitis,	psoriasis, and tropical spastic	paraparesis. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders").	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis. Lyme Disease.
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					asthma and allergy.
154	HE9CP41	1102	SEAP in ATP-3T3- L1		
	HE9CP41	1102	Activation of	Assays for the activation of	A preferred embodiment of
154			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),
				routinely modified to test SRE	Highly preferred indications
				activity of the polypeptides of	include autoimmune diseases
				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,
				antagonists of the invention)	Crohn"s disease, multiple
				include assays disclosed in	sclerosis and/or as described
				Berger et al., Gene 66:1-10	below), immunodeficiencies
				(1998); Cullen and Malm,	(e.g., as described below),
				Methods in Enzymol 216:362-	boosting a T cell-mediated
				368 (1992); Henthorn et al.,	immune response, and
				Proc Natl Acad Sci USA	suppressing a T cell-mediated
				85:6342-6346 (1988); and	immune response. Additional

highly preferred indications include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,
Black et al., Virus Genes 12(2):105-117 (1997) the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.															

					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lympnocyuc anemia (ALL), nlasmacytomas multinle
			,		myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
154	HE9CP41	1102	IL-10 in Human T-cell 2B9		
	HE9CP41	1102	Caspase		
154			(+camptothecin) in		
			SW480		
	HE9DG49	1103	Activation of	Assays for the activation of	Highly preferred indications
155			transcription	transcription through the	include neoplastic diseases
			through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
			response element in	Site (GAS) response element	and/or as described below
			immune cells (such	are well-known in the art and	under "Hyperproliferative

as T-cells).	may be used or routinely	Disorders"). Highly preferred
	modified to assess the ability	indications include neoplasms
	of polypeptides of the	and cancers, such as, for
	invention (including antibodies	example, leukemia, lymphoma
	and agonists or antagonists of	(e.g., T cell lymphoma,
	the invention) to regulate	Burkitt's lymphoma, non-
	STAT transcription factors and	Hodgkins lymphoma,
	modulate gene expression	Hodgkin"s disease),
	involved in a wide variety of	melanoma, and prostate,
-	cell functions. Exemplary	breast, lung, colon, pancreatic,
	assays for transcription	esophageal, stomach, brain,
	through the GAS response	liver and urinary cancer. Other
	element that may be used or	preferred indications include
	routinely modified to test	benign dysproliferative
	GAS-response element activity	disorders and pre-neoplastic
-	of polypeptides of the	conditions, such as, for
-	invention (including antibodies	example, hyperplasia,
	and agonists or antagonists of	metaplasia, and/or dysplasia.
	the invention) include assays	Preferred indications include
	disclosed in Berger et al., Gene	autoimmune diseases (e.g.,
	66:1-10 (1998); Cullen and	rheumatoid arthritis, systemic
	Malm, Methods in Enzymol	lupus erythematosis, multiple
	216:362-368 (1992); Henthorn	sclerosis and/or as described
	et al., Proc Natl Acad Sci USA	below), immunodeficiencies
	85:6342-6346 (1988);	(e.g., as described below),
	Matikainen et al., Blood	boosting a T cell-mediated
	93(6):1980-1991 (1999); and	immune response, and
	Henttinen et al., J Immunol	suppressing a T cell-mediated
	155(10):4582-4587 (1995), the	immune response. Additional
	contents of each of which are	preferred indications include
	herein incorporated by	inflammation and

inflammatory disorders. Highly preferred indications include blood disorders (e.g.,	as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g. viral	infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an	infectious disease as described below under "Infectious Disease"). An additional preferred indication is	idiopathic pulmonary fibrosis.  Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia	(ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia,	neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues,
Exemplary mouse T cells that may be used according to these	assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the CTLL cell line.	which is a suspension culture of IL-2 dependent cytotoxic T cells.				
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for stimulating (e.g., increasing) adipocyte	activation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting the	activation of (e.g., decreasing)	and/or inactivating adipocytes.	Highly preferred indications	include endocrine disorders	(e.g., as described below under	"Endocrine Disorders").	Highly preferred indications	also include neoplastic	diseases (e.g., lipomas,	liposarcomas, and/or as	described below under	"Hyperproliferative	Disorders"). Preferred	indications include blood	disorders (e.g., hypertension,	congestive heart failure, blood	vessel blockage, heart disease,	stroke, impotence and/or as	described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), neural
and agonists or antagonists of the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Le Marchand-	Brustel Y, Exp Clin	Endocrinol Diabetes	107(2):126-132 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Mouse adipocyte cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC).	Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	Implessor a pre-adinocyte to
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disorders (e.g., as described below under "Neural Activity and Neurological Diseases"),	and infection (e.g., as	described below under	"Infectious Disease").	A highly preferred indication	is diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,
adipose-like conversion under appropriate differentiation conditions known in the art.										-																		
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microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below),	neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below (particularly of the urinary tract and skin). An additional highly preferred	indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.  Additional highly preferred indication musculoskeletal systems

including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. Preferred	indications include neoplasms	and cancer, such as,	Iymphoma, leukemia and	breast, colon, and kidney	cancer. Additional preferred	indications include melanoma,	prostate, lung, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer.	Highly preferred indications	include lipomas and	liposarcomas. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	regulation of A highly preferred
					-																								n of Assays for the regulation of
																													1104 Regulation of
				-											•														HE9HY07   1

through the FAS	promoter element are well-	An additional highly preferred
promoter element	known in the art and may be	indication is a complication
 in hepatocytes	used or routinely modified to	associated with diabetes (e.g.,
	assess the ability of	diabetic retinopathy, diabetic
	polypeptides of the invention	nephropathy, kidney disease
	(including antibodies and	(e.g., renal failure,
	agonists or antagonists of the	nephropathy and/or other
	invention) to activate the FAS	diseases and disorders as
	promoter element in a reporter	described in the "Renal
_	construct and to regulate	Disorders" section below),
	transcription of FAS, a key	diabetic neuropathy, nerve
	enzyme for lipogenesis. FAS	disease and nerve damage
	promoter is regulated by many	(e.g., due to diabetic
	transcription factors including	neuropathy), blood vessel
	SREBP. Insulin increases FAS	blockage, heart disease, stroke,
	gene transcription in livers of	impotence (e.g., due to diabetic
	diabetic mice. This	neuropathy or blood vessel
	stimulation of transcription is	blockage), seizures, mental
	also somewhat glucose	confusion, drowsiness,
	dependent. Exemplary assays	nonketotic hyperglycemic-
	that may be used or routinely	hyperosmolar coma,
	modified to test for FAS	cardiovascular disease (e.g.,
	promoter element activity (in	heart disease, atherosclerosis,
	hepatocytes) by polypeptides	microvascular disease,
	of the invention (including	hypertension, stroke, and other
	antibodies and agonists or	diseases and disorders as
	antagonists of the invention)	described in the
	include assays disclosed in	"Cardiovascular Disorders"
	Xiong, S., et al., Proc Natl	section below), dyslipidemia,
	Acad Sci U.S.A., 97(8):3948-	endocrine disorders (as
	53 (2000); Roder, K., et al.,	described in the "Endocrine

				Eur J Biochem. 260(3):743-51	Disorders" section below)
				(1999); Oskoujan B, et al.,	neuropathy, vision impairment
		-		Biochem J, 317 (Pt 1):257-65	(e.g., diabetic retinopathy and
				(1996); Berger, et al., Gene	blindness), ulcers and impaired
				66:1-10 (1988); and, Cullen,	wound healing, and infection
				B., et al., Methods in Enzymol.	(e.g., infectious diseases and
				216:362–368 (1992), the	disorders as described in the
				contents of each of which is	"Infectious Diseases" section
				herein incorporated by	below, especially of the
				reference in its entirety.	urinary tract and skin), carpal
				Hepatocytes that may be used	tunnel syndrome and
				according to these assays, such	Dupuytren's contracture).
•				as H4IIE cells, are publicly	An additional highly preferred
			-	available (e.g., through the	indication is obesity and/or
				ATCC) and/or may be	complications associated with
				routinely generated.	obesity. Additional highly
				Exemplary hepatocytes that	preferred indications include
				may be used according to these	weight loss or alternatively,
				assays include rat liver	weight gain. Aditional
				hepatoma cell line(s) inducible	highly preferred indications are
				with glucocorticoids, insulin,	complications associated with
				or cAMP derivatives.	insulin resistance.
157	HE9NN84	1105	SEAP in 293/ISRE		
	HE9NN84	1105	Activation of	Assays for the activation of	A highly preferred indication
157			transcription	transcription through the	is obesity and/or complications
			through cAMP	cAMP response element are	associated with obesity.
		444	response element	well-known in the art and may	Additional highly preferred
			(CRE) in pre-	be used or routinely modified	indications include weight loss
			adipocytes.	to assess the ability of	or alternatively, weight gain.
				polypeptides of the invention	An additional highly preferred

			(including antibodies and	indication is diabetes mellitus.
			agonists or antagonists of the	An additional highly preferred
			invention) to increase cAMP,	indication is a complication
			regulate CREB transcription	associated with diabetes (e.g.,
			factors, and modulate	diabetic retinopathy, diabetic
			expression of genes involved	nephropathy, kidney disease
			in a wide variety of cell	(e.g., renal failure,
			functions. For example, a	nephropathy and/or other
			3T3-L1/CRE reporter assay	diseases and disorders as
			may be used to identify factors	described in the "Renal
			that activate the cAMP	Disorders" section below),
		٠	signaling pathway. CREB	diabetic neuropathy, nerve
			plays a major role in	disease and nerve damage
			adipogenesis, and is involved	(e.g., due to diabetic
			in differentiation into	neuropathy), blood vessel
			adipocytes. CRE contains the	blockage, heart disease, stroke,
			binding sequence for the	impotence (e.g., due to diabetic
			transcription factor CREB	neuropathy or blood vessel
			(CRE binding protein).	blockage), seizures, mental
			Exemplary assays for	confusion, drowsiness,
			transcription through the	nonketotic hyperglycemic-
			cAMP response element that	hyperosmolar coma,
			may be used or routinely	cardiovascular disease (e.g.,
			modified to test cAMP-	heart disease, atherosclerosis,
			response element activity of	microvascular disease,
			polypeptides of the invention	hypertension, stroke, and other
			(including antibodies and	diseases and disorders as
***			agonists or antagonists of the	described in the
			invention) include assays	"Cardiovascular Disorders"
	,		disclosed in Berger et al., Gene	section below), dyslipidemia,
			66:1-10 (1998); Cullen and	endocrine disorders (as

				Malm, Methods in Enzymol	described in the "Endocrine
				216:362-368 (1992); Henthorn	Disorders" section below),
				et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
·	, , ,			85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
				et al., Mol Cell Biol	blindness), ulcers and impaired
				20(3):1008-1020 (2000); and	wound healing, and infection
				Klemm et al., J Biol Chem	(e.g., infectious diseases and
				273:917-923 (1998), the	disorders as described in the
				contents of each of which are	"Infectious Diseases" section
				herein incorporated by	below, especially of the
				reference in its entirety. Pre-	urinary tract and skin), carpal
				adipocytes that may be used	tunnel syndrome and
				according to these assays are	Dupuytren's contracture).
				publicly available (e.g.,	Additional highly preferred
				through the ATCC) and/or	indications are complications
				may be routinely generated.	associated with insulin
				Exemplary mouse adipocyte	resistance.
				cells that may be used	
				according to these assays	
				include 3T3-L1 cells. 3T3-L1	
				is an adherent mouse	
				preadipocyte cell line that is a	
				continuous substrain of 3T3	
				fibroblast cells developed	
				through clonal isolation and	
				undergo a pre-adipocyte to	
				adipose-like conversion under	
				appropriate differentiation	
				conditions known in the art.	
	HE9NN84	1105	Activation of	This reporter assay measures	Highly preferred indications
157			transcription	activation of the GATA-3	include allergy, asthma, and

through GATA-3	signaling nathway in HMC-1	rhinitis. Additional preferred
ri treemene element in	himon most coll line	indications include infection
	Ilulian mast cen mie.	illuications include illicotion
immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
as mast cells).	cells has been linked to	described below under
	cytokine and chemokine	"Infectious Disease"), and
	production. Assays for the	inflammation and
	activation of transcription	inflammatory disorders.
	through the GATA3 response	Preferred indications also
	element are well-known in the	include blood disorders (e.g.,
	art and may be used or	as described below under
	routinely modified to assess	"Immune Activity", "Blood-
	the ability of polypeptides of	Related Disorders", and/or
	the invention (including	"Cardiovascular Disorders").
	antibodies and agonists or	Preferred indications include
	antagonists of the invention) to	autoimmune diseases (e.g.,
	regulate GATA3 transcription	rheumatoid arthritis, systemic
	factors and modulate	lupus erythematosis, multiple
	expression of mast cell genes	sclerosis and/or as described
	important for immune response	below) and
	development. Exemplary	immunodeficiencies (e.g., as
	assays for transcription	described below). Preferred
	through the GATA3 response	indications include neoplastic
	element that may be used or	diseases (e.g., leukemia,
	routinely modified to test	lymphoma, melanoma,
	GATA3-response element	prostate, breast, lung, colon,
	activity of polypeptides of the	pancreatic, esophageal,
	invention (including antibodies	stomach, brain, liver, and
	and agonists or antagonists of	urinary tract cancers and/or as
	the invention) include assays	described below under
	disclosed in Berger et al., Gene	"Hyperproliferative
	66:1-10 (1998); Cullen and	Disorders"). Other preferred

		Age of the Africa		Malm Methods in Enzymol	indications include henion
				216.362-368 (1992). Henthorn	dysproliferative disorders and
				of al. Deca Matl Acad Cai HGA	ary appropriation conditions and
				et al., Froc Ivall Acad Sci USA	pre-neoplastic conditions, such
				85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
				et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
				Quant Biol 64:563-571 (1999);	Preferred indications include
				Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
				J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
				(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
				Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
				Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
	-			14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
				contents of each of which are	lymphoma, arthritis, AIDS,
				herein incorporated by	granulomatous disease,
	-			reference in its entirety. Mast	inflammatory bowel disease,
				cells that may be used	sepsis, neutropenia,
				according to these assays are	neutrophilia, psoriasis,
_				publicly available (e.g.,	suppression of immune
				through the ATCC).	reactions to transplanted
				Exemplary human mast cells	organs and tissues, hemophilia,
				that may be used according to	hypercoagulation, diabetes
				these assays include the HMC-	mellitus, endocarditis,
				1 cell line, which is an	meningitis, and Lyme Disease.
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
	-			many characteristics of	
				immature mast cells.	
	HE9NN84	1105	Activation of	This reporter assay measures	Highly preferred indications
157			transcription	activation of the NFAT	include allergy, asthma, and

through NFAT signaling pathway in HMC-1 response element in human mast cell line.  as mast cells, cells has been linked to described by production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of assess the ability of including antibodies and autoimmun agonists or antagonists of the invention involved in involved	signaling pathway in HMC-1 human mast cell line.  Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the	rhinitis. Additional preferred	indications include infection	(e.g., an infectious disease as	described below under	Infectious Disease"), and	on and	inflammatory disorders.	Preferred indications also	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described		immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	elow under	iferative	
such	such				described b	"Infectious	inflammation and				as described			"Cardiovas		autoimmun			sclerosis an				indications			prostate, br	pancreatic,			described below under	e   "Hyperproliferative	
through NFAT response element in immune cells (such as mast cells).	through NFAT response element in immune cells (such as mast cells).	signaling pathway in HMC-	human mast cell line.	Activation of NFAT in mast	cells has been linked to	cytokine and chemokine	production. Assays for the	activation of transcription	through the Nuclear Factor of	Activated T cells (NFAT)	response element are well-	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFAT	transcription factors and	modulate expression of gene	involved in	immunomodulatory function	Exemplary assays for	transcription through the	NFAT response element that	may be used or routinely	modified to test NFAT-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	)
		through NFAT	response element in	immune cells (such	as mast cells).																											_

	disclosed in Berger et al. Gene	indications include benion
	66:1-10 (1998); Cullen and	dysproliferative disorders and
	Malm, Methods in Enzymol	pre-neoplastic conditions, such
	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
	85:6342-6346 (1988); De Boer	Preferred indications include
	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
	31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
	et al., J Immunol	leukemias, Hodgkin's disease,
-	165(12):7215-7223 (2000);	acute lymphocytic anemia
	Hutchinson and McCloskey, J	(ALL), plasmacytomas,
	Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
	16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
	al., J Exp Med 188:527-537	granulomatous disease,
	(1998), the contents of each of	inflammatory bowel disease,
	which are herein incorporated	sepsis, neutropenia,
	by reference in its entirety.	neutrophilia, psoriasis,
	Mast cells that may be used	suppression of immune
	according to these assays are	reactions to transplanted
	publicly available (e.g.,	organs and tissues, hemophilia,
	through the ATCC).	hypercoagulation, diabetes
	Exemplary human mast cells	mellitus, endocarditis,
	that may be used according to	meningitis, and Lyme Disease.
	these assays include the HMC-	
	1 cell line, which is an	
	immature human mast cell line	
	established from the peripheral	
	blood of a patient with mast	
	cell leukemia, and exhibits	
	many characteristics of	
	immature mast cells.	

11000	11001170	1106	11 4 60 4 111		
158	ПЕУО W 20	1100	T cells		
	HE90W20	1106	Activation of	Kinase assay. Kinase assays,	Highly preferred indications
158			Skeletal Muscle	for examplek Elk-1 kinase	include endocrine disorders
			Cell ERK	assays, for ERK signal	(e.g., as described below under
			Signalling Pathway	transduction that regulate cell	"Endocrine Disorders") and
				proliferation or differentiation	disorders of the
				are well known in the art and	musculoskeletal system.
				may be used or routinely	Preferred indications include
				modified to assess the ability	neoplastic diseases (e.g., as
				of polypeptides of the	described below under
-				invention (including antibodies	"Hyperproliferative
				and agonists or antagonists of	Disorders"), blood disorders
				the invention) to promote or	(e.g., as described below under
				inhibit cell proliferation,	"Immune Activity",
				activation, and differentiation.	"Cardiovascular Disorders",
				Exemplary assays for ERK	and/or "Blood-Related
				kinase activity that may be	Disorders"), immune disorders
				used or routinely modified to	(e.g., as described below under
		,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,		test ERK kinase-induced	"Immune Activity"), neural
				activity of polypeptides of the	disorders (e.g., as described
				invention (including antibodies	below under "Neural Activity
				and agonists or antagonists of	and Neurological Diseases"),
				the invention) include the	and infection (e.g., as
				assays disclosed in Forrer et	described below under
				al., Biol Chem 379(8-9):1101-	"Infectious Disease"). A
				1110 (1998); Le Marchand-	highly preferred indication is
				Brustel Y, Exp Clin	diabetes mellitus. An
				Endocrinol Diabetes	additional highly preferred
				107(2):126-132 (1999);	indication is a complication
				Kyriakis JM, Biochem Soc	associated with diabetes (e.g.,

	Symp 64:29-48 (1999); Chang	diabetic retinopathy, diabetic
	and Karin, Nature	nephropathy, kidney disease
	   410(6824):37-40 (2001); and	(e.g., renal failure,
 	Cobb MH, Prog Biophys Mol	nephropathy and/or other
	Biol 71(3-4):479-500 (1999);	diseases and disorders as
	the contents of each of which	described in the "Renal
	are herein incorporated by	Disorders" section below),
	reference in its entirety. Rat	diabetic neuropathy, nerve
	myoblast cells that may be	disease and nerve damage
	used according to these assays	(e.g., due to diabetic
	 are publicly available (e.g.,	neuropathy), blood vessel
	through the ATCC).	blockage, heart disease, stroke,
	Exemplary rat myoblast cells	impotence (e.g., due to diabetic
	that may be used according to	neuropathy or blood vessel
	 these assays include L6 cells.	blockage), seizures, mental
	L6 is an adherent rat myoblast	confusion, drowsiness,
	cell line, isolated from primary	nonketotic hyperglycemic-
	 cultures of rat thigh muscle,	hyperosmolar coma,
	that fuses to form	cardiovascular disease (e.g.,
	multinucleated myotubes and	heart disease, atherosclerosis,
	striated fibers after culture in	microvascular disease,
	differentiation media.	hypertension, stroke, and other
		diseases and disorders as
		described in the
 		"Cardiovascular Disorders"
		section below), dyslipidemia,
		endocrine disorders (as
 		described in the "Endocrine
		Disorders" section below),
		neuropathy, vision impairment
		(e.g., diabetic retinopathy and

		blindness), ulcers and impaired
		wound healing, infection (e.g.,
		infectious diseases and
		disorders as described in the
		"Infectious Diseases" section
		below, especially of the
		urinary tract and skin), carpal
		tunnel syndrome and
		Dupuytren's contracture).
		An additional highly preferred
		indication is obesity and/or
		complications associated with
		obesity. Additional highly
		preferred indications include
		weight loss or alternatively,
	,	weight gain. Aditional
		highly preferred indications are
		complications associated with
		insulin resistance.
		Additonal highly preferred
		indications are disorders of the
		musculoskeletal systems
		including myopathies,
		muscular dystrophy, and/or as
		described herein.
		Additional highly preferred
-		indications include: myopathy,
		atrophy, congestive heart
		failure, cachexia, myxomas,
		fibromas, congenital
		cardiovascular abnormalities,

HE9RM63	1107	Activation of transcription through NFKB response element in epithelial cells (such as HELA cells).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB	heart disease, cardiac arrest, heart valve disease, and vascular disease. Highly preferred indications include neoplasms and cancer, such as, rhabdomyoma, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Highly preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.  Preferred embodiments of the invention include using polypeptides of the invention detection, diagnosis, prevention, and/or treatment of Cancer, Wound Healing, and Inflamation. Highly preferred indications include neoplastic
		3	transcription factors and modulate expression of epithhelial genes. Exemplary	diseases (e.g., as described below under "Hyperproliferative

Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, melanoma, and	prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign	dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	referred indications include include inflammatory disorders.
assays for transcription through the NFKB response element that may be used or routinely modified to test	NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays	disclosed in: Kaltschmidt B, et al., Oncogene, 18(21):3213-3225 (1999); Beetz A, et al., Int J Radiat Biol, 76(11):1443-1453 (2000); Berger et al.	Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Epithelial cells that may be used according to these assays are publicly available (e.g.,

160	HEAAR07	1108	Activation of transcription through cAMP response element in immune cells (such as T-cells).	through the ATCC).  Exemplary epithelial cells that may be used according to these assays include the HELA cell line.  Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP and regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. Exemplary assays for transcription the cAMP response element that may be used or routinely modified to test cAMP-response element activity of polypeptides of the invention (including antibodies	Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infectious disease as described below under "Infectious Disease"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional preferred indications include
				and agonists or antagonists of	inflammation and
i				the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998): Cullen and	inflammatory disorders. Highly preferred indications include neonlastic diseases

															-												—		-	
(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma	(e.g., T cell lymphoma,	Burkitt's lymphoma, non-	Hodgkins lymphoma,	Hodgkin"s disease),	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, arthritis,	AIDS, granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,
Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Black et	al., Virus Genes 15(2):105-117	(1997); and Belkowski et al., J	Immunol 161(2):659-665	(1998), the contents of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is a suspension	culture of IL-2 dependent	cytotoxic T cells.											
																			- 38 5 -											

,					suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.
160	HEAAR07	1108	Hexosaminidase in RBL-2H3		
161	HEBAE88	1109	SEAP in 3T3L1		
	HEBAE88	1109	Activation of	Assays for the activation of	Preferred indications include
161			transcription	transcription through the	blood disorders (e.g., as
			through cAMP	cAMP response element are	described below under
			response element in	well-known in the art and may	"Immune Activity", "Blood-
			immune cells (such	be used or routinely modified	Related Disorders", and/or
			as T-cells).	to assess the ability of	"Cardiovascular Disorders"),
				polypeptides of the invention	and infection (e.g., an
				(including antibodies and	infectious disease as described
				agonists or antagonists of the	below under "Infectious
				invention) to increase cAMP	Disease"). Preferred
				and regulate CREB	indications include
				transcription factors, and	autoimmune diseases (e.g.,
				modulate expression of genes	rheumatoid arthritis, systemic
				involved in a wide variety of	lupus erythematosis, multiple
				cell functions. Exemplary	sclerosis and/or as described
				assays for transcription	below), immunodeficiencies
				through the cAMP response	(e.g., as described below),
				element that may be used or	boosting a T cell-mediated
				routinely modified to test	immune response, and
				cAMP-response element	suppressing a T cell-mediated

		activity of polypeptides of the	immune response. Additional
		invention (including antibodies	preferred indications include
		and agonists or antagonists of	inflammation and
		the invention) include assays	inflammatory disorders.
		disclosed in Berger et al., Gene	Highly preferred indications
		66:1-10 (1998); Cullen and	include neoplastic diseases
•		Malm, Methods in Enzymol	(e.g., leukemia, lymphoma,
		216:362-368 (1992); Henthorn	and/or as described below
		et al., Proc Natl Acad Sci USA	under "Hyperproliferative
		85:6342-6346 (1988); Black et	Disorders"). Highly preferred
,		al., Virus Genes 15(2):105-117	indications include neoplasms
		(1997); and Belkowski et al., J	and cancers, such as, for
		Immunol 161(2):659-665	example, leukemia, lymphoma
		(1998), the contents of each of	(e.g., T cell lymphoma,
		which are herein incorporated	Burkitt's lymphoma, non-
		by reference in its entirety. T	Hodgkins lymphoma,
		cells that may be used	Hodgkin"s disease),
		according to these assays are	melanoma, and prostate,
		publicly available (e.g.,	breast, lung, colon, pancreatic,
		through the ATCC).	esophageal, stomach, brain,
		Exemplary mouse T cells that	liver and urinary cancer. Other
		may be used according to these	preferred indications include
		assays include the CTLL cell	benign dysproliferative
		line, which is a suspension	disorders and pre-neoplastic
		culture of IL-2 dependent	conditions, such as, for
		cytotoxic T cells.	example, hyperplasia,
			metaplasia, and/or dysplasia.
			Preferred indications include
			anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			acute lymphocytic anemia

(ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.		Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of asthma, allergy, hypersensitivity and inflammation.
		Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate caspase protease-mediated apoptosis in immune cells (such as, for example, in mast cells). Mast cells are found in connective and mucosal tissues throughout the body, and their activation via immunoglobulin E.
	SEAP in OE-33	Regulation of apoptosis of immune cells (such as mast cells).
	1109	1110
	HEBAE88	HEBBN36
	161	79

antigen, promoted by T helper cell type 2 cytokines, is an important component of allergic disease. Dysregulation of mast cell apoptosis may	play a role in allergic disease and mast cell tumor survival.  Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity	induced by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Masuda A, et al., J Biol Chem,	Yeatman CF 2nd, et al., J Exp Med, 192(8):1093-1103 (2000);Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209- 218 (2000); and Karsan and	Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are
ar ce ce in in in all all all all all all all all all al	ple and	in i	2.7 Y. Y. W. W. (2.2)	HH (1) (2) (3) (3) (4) (4) (4) (4) (4) (4) (4) (4) (4) (4

[5]	publicly available (e.g., through commercial sources).	Exemplary immune cells that	may be used according to these	assays include mast cells such	as the HMC human mast cell		Assays for the activation of Highly preferred indications	transcription through the include asthma, allergy,	Gamma Interferon Activation hypersensitivity reactions,	Site (GAS) response element   inflammation, and	are well-known in the art and inflammatory disorders.	may be used or routinely Additional highly preferred	modified to assess the ability indications include immune	of polypeptides of the and hematopoietic disorders	invention (including antibodies   (e.g., as described below under		the invention) to modulate "Blood-Related Disorders"),	gene expression (commonly autoimmune diseases (e.g.,	via STAT transcription factors)   rheumatoid arthritis, systemic	involved in a wide variety of   lupus erythematosis, Crohn"s	cell functions. Exemplary disease, multiple sclerosis		through the GAS response   immunodeficiencies (e.g., as	element that may be used or described below), boosting an	routinely modified to test eosinophil-mediated immune	GAS-response element activity   response and, alternatively,	of polypeptides of the suppressing an eosinophil-	invention (including antibodies   mediated immune response.	and agonists or antagonists of	•
11	thron	Exen	may	assay	as th	line.	Activation of Assa	transcription trans	through GAS Gam	response element in   Site (	immune cells (such   are w	as eosinophils).	ipom	od bo	inver	and a	the ir	gene	via S	ovni	cell f	assay	thron	elem	routi	GAS	od Jo	inver	and a	
							HEBCM63   1111																							_
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disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthom et al., Proc Natl Acad Sci USA 85:6342-6346 (1988);	Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995); the contents of each of which are berein incorporated by.	reference in its entirety.  Moreover, exemplary assays that may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies	and agonists or antagonists of the invention) to activate or inhibit activation of immune cells include assays disclosed and/or cited in: Mayumi M., "EoL-1, a human eosinophilic	Jun;7(3):243-50 (1992); Bhattacharya S, "Granulocyte macrophage colonystimulating factor and interleukin-5 activate STAT5 and induce CIS1 mRNA in

		A highly preferred embodiment of the invention includes a method for
human peripheral blood eosinophils." Am J Respir Cell Mol Biol; Mar;24(3):312-6 (2001); and, Du J, et al., "Engagement of the CrkL adapter in interleukin-5 signaling in eosinophils." J Biol Chem; Oct 20;275(42):33167-75 (2000); the contents of each of which are herein incorporated by reference in its entirety. Exemplary cells that may be used according to these assays include eosinophils. Eosinophils are a type of immune cell important in the late stage of allergic reactions; they are recruited to tissues and mediate the inflammtory response of late stage allergic reaction. Increases in GAS mediated transcription in eosinophils is typically a result of STAT activation, normally a direct consequence of	interleukin or other cytokine receptor stimulation (e.g. IL3, IL5 or GMCSF).	T. IFNg plays he immune usidered to be
		Production of IFNgamma using a T cells
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		HEBCM63
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stimulating the production of IFNg. An alternative highly	preferred embodiment of the invention includes a method	for inhibiting the production of	IFNg. Highly preferred		disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or as	described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune disease (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiency	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional
a proinflammatory cytokine. IFNg promotes TH1 and	inhibits TH2 differentiation; promotes IgG2a and inhibits	IgE secretion; induces	macrophage activation; and	increases MHC expression.	Assays for immunomodulatory	proteins produced by T cells	and NK cells that regulate a	variety of inflammatory	activities and inhibit TH2	helper cell functions are well	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, regulate	inflammatory activities,	modulate TH2 helper cell	function, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays	that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as Interferon	gamma (IFNg), and the
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								-			200																	

activation of T cells. Such	highly preferred indications
assays that may be used or	include inflammation and
routinely modified to test	inflammatory disorders.
immunomodulatory activity of	Additional preferred
polypeptides of the invention	indications include idiopathic
(including antibodies and	pulmonary fibrosis. Highly
agonists or antagonists of the	preferred indications include
 invention) include the assays	neoplastic diseases (e.g.,
disclosed in Miraglia et al., J	leukemia, lymphoma,
Biomolecular Screening 4:193-	melanoma, and/or as described
204 (1999); Rowland et al.,	below under
"Lymphocytes: a practical	"Hyperproliferative
approach" Chapter 6:138-160	Disorders"). Highly preferred
(2000); Gonzalez et al., J Clin	indications include neoplasms
Lab Anal 8(5):225-233 (1995);	and cancers, such as, for
Billiau et al., Ann NY Acad	example, leukemia, lymphoma,
Sci 856:22-32 (1998); Boehm	melanoma, and prostate,
et al., Annu Rev Immunol	breast, lung, colon, pancreatic,
15:749-795 (1997), and	esophageal, stomach, brain,
Rheumatology (Oxford)	liver and urinary cancer. Other
38(3):214-20 (1999), the	preferred indications include
contents of each of which are	benign dysproliferative
herein incorporated by	disorders and pre-neoplastic
reference in its entirety.	conditions, such as, for
Human T cells that may be	example, hyperplasia,
used according to these assays	metaplasia, and/or dysplasia.
may be isolated using	Preferred indications include
techniques disclosed herein or	anemia, pancytopenia,
otherwise known in the art.	leukopenia, thrombocytopenia,
Human T cells are primary	Hodgkin's disease, acute
human lymphocytes that	lymphocytic anemia (ALL).

mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance immunomodulatory factors.  mature in the thymus and myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	Kinase assay. JNK and p38  Kinase assays for signal kinase assays for signal kinase assays for signal kinase assays for signal proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of antibodies and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit immune cell (e.g. T-cell) proliferation, and apoptosis.  Exemplary assays for JNK and autoimmune diseases (e.g., p38 kinase activity that may be rest INK and n38 kinase-
matu expression of the control of th	Activation of T-  Cell p38 or JNK kinas Signaling Pathway. prolii apopt the al routiin the al the ir antib antag prom (e.g. activa Exem p38 k
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	HEBEJ18
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below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Highly preferred indications	also include neoplastic	diseases (e.g., leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	arthritis, asthma, AIDS,	allergy, anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin"s disease, acute	lymphocytic anemia (ALL).
induced activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Forrer et al., Biol	Chem 379(8-9):1101-1110	(1998); Gupta et al., Exp Cell	Res 247(2): 495-504 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension-culture	cell line with cytotoxic	activity.		
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					piasmacytomas, mulippie myeloma, Burkitt's lymphoma,
					granulomatous disease,
		1			inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
_		,			transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HEEAG23	1113	Activation of	Kinase assay. Kinase assays,	A highly preferred
		#	Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
_			Signaling Pathway	assay, for ERK signal	includes a method for
				transduction that regulate cell	stimulating adipocyte
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment
	,	<b>113</b>		may be used or routinely	of the invention includes a
				modified to assess the ability	method for inhibiting
				of polypeptides of the	adipocyte proliferation. A
				invention (including antibodies	highly preferred embodiment
				and agonists or antagonists of	of the invention includes a
				the invention) to promote or	method for stimulating
				inhibit cell proliferation,	adipocyte differentiation. An
				activation, and differentiation.	alternative highly preferred
				Exemplary assays for ERK	embodiment of the invention
				kinase activity that may be	includes a method for
				used or routinely modified to	inhibiting adipocyte
				test ERK kinase-induced	differentiation. A highly
				activity of polypeptides of the	preferred embodiment of the
				invention (including antibodies	invention includes a method
				and agonists or antagonists of	for stimulating (e.g.,
				the invention) include the	increasing) adipocyte

olosib svesse	assavs disclosed in Forrer et	ectivation An alternative
accept accept accept and the proof of the pr	al Biol Cham 270/8 0):1101	highly anothernal and discout
ali, Diol Cile	111 5/5(8-9):1101-	nigniy preferred embodiment
(1110 (1998))	1110 (1998); Le Marchand-	of the invention includes a
Brustel Y, Exp Clin	kp Clin	method for inhibiting the
Endocrinol Diabetes	Diabetes	activation of (e.g., decreasing)
107(2):126-132 (1999);	32 (1999);	and/or inactivating adipocytes.
Kyriakis JM.	Kyriakis JM, Biochem Soc	Highly preferred indications
Symp 64:29-	Symp 64:29-48 (1999); Chang	include endocrine disorders
and Karin, Nature	ature	(e.g., as described below under
410(6824):3	410(6824):37-40 (2001); and	"Endocrine Disorders").
Cobb MH, P	Cobb MH, Prog Biophys Mol	Highly preferred indications
Biol 71(3-4):	Biol 71(3-4):479-500 (1999);	also include neoplastic
the contents	the contents of each of which	diseases (e.g., lipomas,
are herein in	are herein incorporated by	liposarcomas, and/or as
reference in its entirety.	ts entirety.	described below under
Mouse adipo	Mouse adipocyte cells that	"Hyperproliferative
may be used	may be used according to these	Disorders"). Preferred
assays are pu	assays are publicly available	indications include blood
(e.g., through	(e.g., through the ATCC).	disorders (e.g., hypertension,
Exemplary n	Exemplary mouse adipocyte	congestive heart failure, blood
cells that may be used	y be used	vessel blockage, heart disease,
according to these assays	these assays	stroke, impotence and/or as
include 3T3-	include 3T3-L1 cells. 3T3-L1	described below under
is an adherent mouse	t mouse	"Immune Activity",
preadipocyte	preadipocyte cell line that is a	"Cardiovascular Disorders",
continuous si	continuous substrain of 3T3	and/or "Blood-Related
fibroblast cells developed	ls developed	Disorders"), immune disorders
through clon	through clonal isolation and	(e.g., as described below under
undergo a pre	undergo a pre-adipocyte to	"Immune Activity"), neural
adipose-like	adipose-like conversion under	disorders (e.g., as described
appropriate d	appropriate differentiation	below under "Neural Activity

conditions known in the art.	and Neurological Diseases"),	and infection (e.g., as	described below under	"Infectious Disease").	A highly preferred indication	is diabetes mellitus.	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other
	conditions known in the art.												***	-																	
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diseases and disorders as described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as
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	HEEAG23	1113	Activation of	Kinase assay. Kinase assays,	A highly preferred
165	-		Skeletal Mucle Cell	for example an GSK-3 kinase	embodiment of the invention
			PI3 Kinase	assay, for PI3 kinase signal	includes a method for
			Signalling Pathway	transduction that regulate	increasing muscle cell survival
				glucose metabolism and cell	An alternative highly preferred
				survivial are well-known in the	embodiment of the invention
				art and may be used or	includes a method for
				routinely modified to assess	decreasing muscle cell
	, ,			the ability of polypeptides of	survival. A preferred
				the invention (including	embodiment of the invention
				antibodies and agonists or	includes a method for
				antagonists of the invention) to	stimulating muscle cell
				promote or inhibit glucose	proliferation. In a specific
				metabolism and cell survival.	embodiment, skeletal muscle
				Exemplary assays for PI3	cell proliferation is stimulated.
				kinase activity that may be	An alternative highly preferred
				used or routinely modified to	embodiment of the invention
				test PI3 kinase-induced activity	includes a method for
				of polypeptides of the	inhibiting muscle cell
				invention (including antibodies	proliferation. In a specific
				and agonists or antagonists of	embodiment, skeletal muscle
				the invention) include assays	cell proliferation is inhibited.
				disclosed in Forrer et al., Biol	A preferred embodiment of
				Chem 379(8-9):1101-1110	the invention includes a
				(1998); Nikoulina et al.,	method for stimulating muscle
				Diabetes 49(2):263-271	cell differentiation. In a
				(2000); and Schreyer et al.,	specific embodiment, skeletal
				Diabetes 48(8):1662-1666	muscle cell differentiation is
				(1999), the contents of each of	stimulated. An alternative
				which are herein incorporated	highly preferred embodiment
				by reference in its entirety.	of the invention includes a

method for inhibiting muscle cell differentiation. In a specific embodiment, skeletal muscle cell differentiation is inhibited. Highly preferred	indications include disorders of the musculoskeletal system. Preferred indications include	neoplastic diseases (e.g., as described below under "Hyperproliferative"	Disorders'), endocrine disorders (e.g., as described below under "Endocrine"	Disorders"), neural disorders (e.g., as described below under	"Neural Activity and Neurological Diseases"), blood	disorders (e.g., as described below under "Immune	Activity", "Cardiovascular Disorders", and/or "Blood-	Related Disorders"), immune disorders (e.g., as described	below under "Immune Activity"), and infection (e.g.	as described below under	"Infectious Disease"). A	highly preferred indication is diabetes mellitus. An additional highly preferred
Rat myoblast cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary rat myoblast cells	that may be used according to these assays include L6 cells. L6 is an adherent rat myoblast	cell line, isolated from primary cultures of rat thigh muscle, that fuses to form	munnucleated myonoes and striated fibers after culture in differentiation media.									

indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage (e.g.,	due to diabetic neuropathy),	blood vessel blockage, heart	disease, stroke, impotence	(e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),
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		neuropathy, vision impairment
		(e.g., diabetic retinopathy and
	-	blindness), ulcers and impaired
		wound healing, infections
		(e.g., infectious diseases and
		disorders as described in the
		"Infectious Diseases" section
	-	below, especially of the
		urinary tract and skin), carpal
-		tunnel syndrome and
		Dupuytren's contracture).
		An additional highly preferred
		indication is obesity and/or
	******	complications associated with
	- A	obesity. Additional highly
		preferred indications include
		weight loss or alternatively,
		weight gain. Additional
		highly preferred indications are
		complications associated with
		insulin resistance.
		Additonal highly preferred
		indications are disorders of the
		musculoskeletal system
		including myopathies,
		muscular dystrophy, and/or as
		described herein.
		Additional highly preferred
		indications include: myopathy,
		atrophy, congestive heart
		failure, cachexia, myxomas,

fibromas, congenital cardiovascular abnormalities, heart disease, cardiac arrest, heart valve disease, and vascular disease. Highly preferred indications include neoplasms and cancer, such as, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.			f AP1 vn in	the art and may be used or "Hyperproliterative routinely modified to assess") blood disorders	
					the ability of polypeptides of
	SEAP in OE-33	SEAP in 3T3L1	Activation of transcription through AP1	response element in immune cells (such	
	1113	1114	1114		
	HEEAG23	HEEAJ02	HEEAJ02		
	165	166	166		_

		antibodies and agonists or	"Cardiovascular Disorders",
		antagonists of the invention) to	and/or "Blood-Related
	·	modulate growth and other cell	Disorders"), and infection
-		functions. Exemplary assays	(e.g., an infectious disease as
		for transcription through the	described below under
		AP1 response element that	"Infectious Disease"). Highly
		may be used or routinely	preferred indications include
		modified to test AP1-response	autoimmune diseases (e.g.,
		element activity of	rheumatoid arthritis, systemic
		polypeptides of the invention	lupus erythematosis, multiple
		(including antibodies and	sclerosis and/or as described
		agonists or antagonists of the	below) and
		invention) include assays	immunodeficiencies (e.g., as
		disclosed in Berger et al., Gene	described below). Additional
		66:1-10 (1988); Cullen and	highly preferred indications
		Malm, Methods in Enzymol	include inflammation and
		216:362-368 (1992); Henthorn	inflammatory disorders.
		et al., Proc Natl Acad Sci USA	Highly preferred indications
		85:6342-6346 (1988);	also include neoplastic
	4.	Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
		272(49):30806-30811 (1997);	lymphoma, and/or as described
		Chang et al., Mol Cell Biol	below under
		18(9):4986-4993 (1998); and	"Hyperproliferative
		Fraser et al., Eur J Immunol	Disorders"). Highly preferred
		29(3):838-844 (1999), the	indications include neoplasms
		contents of each of which are	and cancers, such as, leukemia,
		herein incorporated by	lymphoma, prostate, breast,
		reference in its entirety. T	lung, colon, pancreatic,
		cells that may be used	esophageal, stomach, brain,
		according to these assays are	liver, and urinary cancer. Other
		publicly available (e.g.,	preferred indications include

benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood
through the ATCC).  Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response
	Activation of transcription through serum response element in immune cells (such as T-cells).
	1114
	HEEAJ02
	166

factors and modulate the		disorders (e.g., as described
expression of genes involved	lved	below under "Immune
in growth. Exemplary assays		Activity", "Blood-Related
for transcription through the	the	Disorders", and/or
SRE that may be used or		"Cardiovascular Disorders"),
routinely modified to test SRE		Highly preferred indications
activity of the polypeptides of		include autoimmune diseases
the invention (including		(e.g., rheumatoid arthritis,
antibodies and agonists or		systemic lupus erythematosis,
antagonists of the invention)		Crohn"s disease, multiple
include assays disclosed in		sclerosis and/or as described
Berger et al., Gene 66:1-10	·	below), immunodeficiencies
(1998); Cullen and Malm,		(e.g., as described below),
Methods in Enzymol 216:362-		boosting a T cell-mediated
368 (1992); Henthorn et al.,		immune response, and
Proc Natl Acad Sci USA		suppressing a T cell-mediated
85:6342-6346 (1988); and		immune response. Additional
Black et al., Virus Genes		highly preferred indications
12(2):105-117 (1997), the		include inflammation and
content of each of which are		inflammatory disorders, and
herein incorporated by		treating joint damage in
reference in its entirety.		patients with rheumatoid
cells that may be used	arthr	arthritis. An additional highly
according to these assays are	's are	preferred indication is sepsis.
publicly available (e.g.,		Highly preferred indications
through the ATCC).		include neoplastic diseases
Exemplary mouse T cells that	-	(e.g., leukemia, lymphoma,
may be used according to these		and/or as described below
assays include the CTLL cell		under "Hyperproliferative
line, which is an IL-2		Disorders"). Additionally,
dependent suspension culture		highly preferred indications

		of T cells with cytotoxic	include neoplasms and
		activity.	cancers, such as, for example,
-			leukemia, lymphoma,
			melanoma, glioma (e.g.,
			malignant glioma), solid
			tumors, and prostate, breast,
			lung, colon, pancreatic,
			esophageal, stomach, brain,
			liver and urinary cancer. Other
			preferred indications include
			benign dysproliferative
			disorders and pre-neoplastic
************			conditions, such as, for
	•		example, hyperplasia,
			metaplasia, and/or dysplasia.
	•		Preferred indications include
			anemia, pancytopenia,
	Mark States		leukopenia, thrombocytopenia,
			Hodgkin's disease, acute
			lymphocytic anemia (ALL),
			plasmacytomas, multiple
			myeloma, Burkitt's lymphoma,
			arthritis, AIDS, granulomatous
			disease, inflammatory bowel
			disease, neutropenia,
			neutrophilia, psoriasis,
			suppression of immune
			reactions to transplanted
			organs and tissues,
			hemophilia, hypercoagulation,
			diabetes mellitus, endocarditis,

meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	
	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. 3T3-L1 is a mouse preadinocyte cell line. It
	Proliferation of preadipose cells (such as 3T3-L1 cells)
	1114
	HEEAJ02
	166

		<u>.</u>
		Highly preferred indications include eosinophilia, asthma, allergy, hypersensitivity reactions, inflammation, and inflammatory disorders.  Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), Highly
is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127-133 (1974), which is herein incorporated by reference in its entirety.		Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of eosinophil cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be
	SEAP in Jurkat/IL4 promoter (antiCD3 co-stim)	Regulation of viability or proliferation of immune cells (such as human eosinophil EOL-1 cells).
	1114	1115
	HEEAJ02	HEEAQ11
	166	167

				viable cells in culture based on	preferred indications also
	***			quantitation of the ATP	include boosting or inhibiting
				present which signals the	immune cell proliferation.
				presence of metabolically	Preferred indications include
				active cells. Eosinophils are a	neoplastic diseases (e.g.,
			-	type of immune cell important	leukemia, lymphoma, and/or as
<del>.</del>				in allergic responses; they are	described below under
				recruited to tissues and	"Hyperproliferative
-				mediate the inflammtory	Disorders"). Highly preferred
				response of late stage allergic	indications include boosting an
				reaction. Eosinophil cell lines	eosinophil-mediated immune
				that may be used according to	response, and suppressing an
				these assays are publicly	eosinophil-mediated immune
				available and/or may be	response.
				routinely generated.	
				Exemplary eosinophil cells	
				that may be used according to	
	Pur			these assays include EOL-1	
				Cells.	
	HEEAQ11	11115	Activation of T-	Kinase assay. JNK and p38	Preferred indications include
167			Cell p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as
			Signaling Pathway.	transduction that regulate cell	described below under
				proliferation, activation, or	"Hyperproliferative
				apoptosis are well known in	Disorders"), blood disorders
				the art and may be used or	(e.g., as described below under
				routinely modified to assess	"Immune Activity",
				the ability of polypeptides of	"Cardiovascular Disorders",
				the invention (including	and/or "Blood-Related
				antibodies and agonists or	Disorders"), and infection
				antagonists of the invention) to	(e.g., an infectious disease as
			1.00	promote or inhibit immune cell	described below under

(e o T-cell) proliferation	"Infections Diseases") Highly
(c.g. 1 con) promoranon,	micendas Disease ). mgmy
acuvation, and apoptosis.	preferred indications include
 Exemplary assays for JNK and	autoimmune diseases (e.g.,
p38 kinase activity that may be	rheumatoid arthritis, systemic
used or routinely modified to	lupus erythematosis, multiple
test JNK and p38 kinase-	sclerosis and/or as described
induced activity of	below) and
polypeptides of the invention	immunodeficiencies (e.g., as
(including antibodies and	described below). Additional
agonists or antagonists of the	highly preferred indications
invention) include the assays	include inflammation and
disclosed in Forrer et al., Biol	inflammatory disorders.
Chem 379(8-9):1101-1110	Highly preferred indications
(1998); Gupta et al., Exp Cell	also include neoplastic
Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
Kyriakis JM, Biochem Soc	lymphoma, and/or as described
Symp 64:29-48 (1999); Chang	below under
and Karin, Nature	"Hyperproliferative
 410(6824):37-40 (2001); and	Disorders"). Highly preferred
Cobb MH, Prog Biophys Mol	indications include neoplasms
Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
the contents of each of which	lymphoma, prostate, breast,
are herein incorporated by	lung, colon, pancreatic,
reference in its entirety. T	esophageal, stomach, brain,
cells that may be used	liver, and urinary cancer. Other
according to these assays are	preferred indications include
publicly available (e.g.,	benign dysproliferative
through the ATCC).	disorders and pre-neoplastic
Exemplary mouse T cells that	conditions, such as, for
may be used according to these	example, hyperplasia,
assays include the CTLL cell	metaplasia, and/or dysplasia.

				line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.	Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin"s disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt"s lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.
167	HEEAQ11	1115	CD71 in Human T cells		
168	HEEBIOS	1116	Activation of transcription through NFAT response element in immune cells (such as mast cells).	This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or

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"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	''Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	
assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFAT	transcription factors and	modulate expression of genes	involved in	immunomodulatory functions.	Exemplary assays for	transcription through the	NFAT response element that	may be used or routinely	modified to test NFAT-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); De Boer	et al., Int J Biochem Cell Biol	31(10):1221-1236 (1999); Ali	et al., J Immunol	165(12):7215-7223 (2000);	Hutchinson and McCloskey, J	1000 F
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							-																							
																	•						-							

lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell
al., J Exp Med 188:527-537 (1998), the contents of each of which are herein incorporated by reference in its entirety.  Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Induction of apoptosis in endothelial cells supporting the
	Endothelial Cell Apoptosis
	1117
	НЕGАН43
	169

		vasculature of tumors is	proliferation. An alternative
	•	associated with tumor	highly preferred embodiment
		regression due to loss of tumor	
		blood supply. Exemplary	method for inhibiting
		assays for caspase apoptosis	endothelial cell proliferation.
		that may be used or routinely	A highly preferred
		modified to test capase	embodiment of the invention
		apoptosis activity of	includes a method for
-		polypeptides of the invention	stimulating apoptosis of
		(including antibodies and	endothelial cells. An
		agonists or antagonists of the	alternative highly preferred
		invention) include the assays	embodiment of the invention
		disclosed in Lee et al., FEBS	
		Lett 485(2-3): 122-126 (2000);	
		Nor et al., J Vasc Res 37(3):	apoptosis of endothelial cells.
-1		209-218 (2000); and Karsan	A highly preferred
		and Harlan, J Atheroscler	embodiment of the invention
		Thromb 3(2): 75-80 (1996);	includes a method for
		the contents of each of which	stimulating angiogenisis. An
		are herein incorporated by	alternative highly preferred
		reference in its entirety.	embodiment of the invention
		Endothelial cells that may be	includes a method for
		used according to these assays	inhibiting angiogenesis. A
		are publicly available (e.g.,	highly preferred embodiment
		through commercial sources).	of the invention includes a
		Exemplary endothelial cells	method for reducing cardiac
		that may be used according to	hypertrophy. An alternative
		these assays include bovine	highly preferred embodiment
		aortic endothelial cells	of the invention includes a
		(bAEC), which are an example	method for inducing cardiac
		of endothelial cells which line	hypertrophy. Highly

		and atherosclerotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders").	Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that
blood vessels and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone,	and immune cell extravasation.		
	•		

stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization.	Highly preferred indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal disorders. Highly preferred indications	include neoplasms and cancer, such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma,	haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neonlastic conditions, such

as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease.	such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud''s	disease and Reynaud"s phenomenom, aneurysms, restenosis; venous and lymphatic disorders such as thrombophlebitis,	lymphangitis, and lymphedema; and other vascular disorders such as peripheral vascular disease,	and cancer. Highly preferred indications also include trauma such as wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from	balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal

Additional highly preferred	indications include stroke, or oraft rejection dishetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	preferred indications include

inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.		Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of agonists or antagonists of the invention detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular invention) to regulate ICAM-1 Disease, Athereosclerosis, expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its	entirety Celle that may be
	SEAP in HIB/CRE	Production of Assa   ICAM-1   well- be us to ass polyr (inch agon) inven expre that n modi expre discle   FASI (2001) al., A   1739   each each each each each each each each	entire
•	, 1117	1118	
	HEGAH43	HEGAN94	
`	169	170	

				1111	
				through the ATCC) and/or	
				may be routinely generated.	
				Exemplary cells that may be	
				used according to these assays	
<b>.</b>				include microvascular	
				endothelial cells (MVEC).	
170	HEGAN94	1118	ICAM in 0E19		
	HEGBS69	1119	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
171				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
	-			participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
	-			role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
	P			Deregulated expression of IL-6	reducing) IL-6 production. A
				has been linked to autoimmune	highly preferrred indication is
				disease, plasmacytomas,	the stimulation or enhancement
				myelomas, and chronic	of mucosal immunity. Highly
				hyperproliferative diseases.	preferred indications include
				Assays for immunomodulatory	blood disorders (e.g., as
				and differentiation factor	described below under
				proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
		78871		expression level is strongly	"Cardiovascular Disorders"),
				regulated by cytokines, growth	and infection (e.g., as
			-	factors, and hormones are well	described below under
				known in the art and may be	"Infectious Disease"). Highly
				used or routinely modified to	preferred indications include

		assess the ability of	autoimmune diseases (e.g
		polypeptides of the invention	rheumatoid arthritis, systemic
		(including antibodies and	lupus erythematosis, multiple
		agonists or antagonists of the	sclerosis and/or as described
		invention) to mediate	below) and
		immunomodulation and	immunodeficiencies (e.g., as
		differentiation and modulate T	described below). Highly
-		cell proliferation and function.	preferred indications also
		Exemplary assays that test for	include boosting a B cell-
		immunomodulatory proteins	mediated immune response
		evaluate the production of	and alternatively suppressing a
		cytokines, such as IL-6, and	B cell-mediated immune
		the stimulation and	response. Highly preferred
		upregulation of T cell	indications include
		proliferation and functional	inflammation and
		activities. Such assays that	inflammatory
		may be used or routinely	disorders.Additional highly
		modified to test	preferred indications include
		immunomodulatory and	asthma and allergy. Highly
		diffferentiation activity of	preferred indications include
		polypeptides of the invention	neoplastic diseases (e.g.,
		(including antibodies and	myeloma, plasmacytoma,
	744	agonists or antagonists of the	leukemia, lymphoma,
		invention) include assays	melanoma, and/or as described
		disclosed in Miraglia et al., J	below under
		Biomolecular Screening 4:193-	"Hyperproliferative
		204(1999); Rowland et al.,	Disorders"). Highly preferred
		"Lymphocytes: a practical	indications include neoplasms
		approach" Chapter 6:138-160	and cancers, such as, myeloma,
		(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
		Immunol 158: 2919-2925	lymphoma, melanoma, and

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prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and	urinary cancer. Other preferred indications include benign dysproliferative disorders and	pre-neoplastic conditions, such as, for example, hyperplasia, metanlasia, and/or dyenlasia.	Preferred indications include anemia, pancytopenia,	leukopenia, thrombocytopenia, Hodgkin's disease, acute	lymphocytic anemia (ALL),	Inuliple myeloma, Burkitt's lymphoma, arthritis, AIDS,	granulomatous disease, inflammatory bowel disease	sepsis, neutropenia,	neutrophilia, psoriasis, suppression of immune	reactions to transplanted	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, and Lyme Disease. An additional preferred	indication is infection (e.g., an	infectious disease as described	below under "Infectious
(1997), the contents of each of which are herein incorporated by reference in its entirety.	Human dendritic cells that may be used according to these assays may be isolated using	techniques disclosed herein or otherwise known in the art. Human dendritic cells are	antigen presenting cells in suspension culture, which.	when activated by antigen and/or cytokines, initiate and	upregulate T cell proliferation	and tunctional activities.										
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171	HEGBS69	1119	CD152 in Human T cells		
,	HELGK31	1120	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
172	<del></del>			by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
			-	IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
	,			Deregulated expression of IL-6	reducing) IL-6 production. A
				has been linked to autoimmune	highly preferrred indication is
				disease, plasmacytomas,	the stimulation or enhancement
				myelomas, and chronic	of mucosal immunity. Highly
				hyperproliferative diseases.	preferred indications include
27				Assays for immunomodulatory	blood disorders (e.g., as
			-	and differentiation factor	described below under
				proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
				expression level is strongly	"Cardiovascular Disorders"),
				regulated by cytokines, growth	and infection (e.g., as
				factors, and hormones are well	described below under
				known in the art and may be	"Infectious Disease"). Highly
				used or routinely modified to	preferred indications include
_				assess the ability of	autoimmune diseases (e.g.,
		-		polypeptides of the invention	rheumatoid arthritis, systemic
				(including antibodies and	lupus erythematosis, multiple
		-		agonists or antagonists of the	sclerosis and/or as described
				invention) to mediate	below) and
			•	immunomodulation and	immunodeficiencies (e.g., as
				differentiation and modulate T	described below). Highly

cell proliferation and function. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-6, and the stimulation and upregulation of T cell proliferation and functional activities. Such assays that may be used or routinely modified to test immunomodulatory and differentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these
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otherwise known in the art.  Human dendritic cells are antigen presenting cells in Preferred indications include suspension culture, which, when activated by antigen Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infectious by pieces."	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; preferred embodiment of the promotes IgG2a and inhibits
Human antigen suspen:  when a and/or upregu and fur	IFNgarma using a a central real system a proin IFNg p inhibits
	1120
	HELGK31
	172

IgE secretion; induces macrophage activation; and	for inhibiting the production of IFNo Highly preferred
increases MHC expression.	ions
Assays for immunomodulatory	disorders (e.g., as described
proteins produced by T cells	below under "Immune
and NK cells that regulate a	Activity", "Blood-Related
variety of inflammatory	Disorders", and/or
activities and inhibit TH2	"Cardiovascular Disorders"),
helper cell functions are well	and infection (e.g., viral
known in the art and may be	infections, tuberculosis,
used or routinely modified to	infections associated with
assess the ability of	chronic granulomatosus
 polypeptides of the invention	disease and malignant
 (including antibodies and	osteoporosis, and/or as
agonists or antagonists of the	described below under
invention) to mediate	"Infectious Disease"). Highly
immunomodulation, regulate	preferred indications include
inflammatory activities,	autoimmune disease (e.g.,
modulate TH2 helper cell	rheumatoid arthritis, systemic
function, and/or mediate	lupus erythematosis, multiple
 humoral or cell-mediated	sclerosis and/or as described
immunity. Exemplary assays	below), immunodeficiency
that test for	(e.g., as described below),
 immunomodulatory proteins	boosting a T cell-mediated
 evaluate the production of	immune response, and
 cytokines, such as Interferon	suppressing a T cell-mediated
gamma (IFNg), and the	immune response. Additional
activation of T cells. Such	highly preferred indications
 assays that may be used or	include inflammation and
routinely modified to test	inflammatory disorders.
immunomodulatory activity of	Additional preferred

	polypeptides of the invention	indications include idiopathic
	(including antibodies and	pulmonary fibrosis. Highly
-	agonists or antagonists of the	preferred indications include
	invention) include the assays	neoplastic diseases (e.g.,
	disclosed in Miraglia et al., J	leukemia, lymphoma,
	Biomolecular Screening 4:193-	melanoma, and/or as described
	204 (1999); Rowland et al.,	below under
	"Lymphocytes: a practical	"Hyperproliferative
	approach" Chapter 6:138-160	Disorders"). Highly preferred
	(2000); Gonzalez et al., J Clin	indications include neoplasms
	Lab Anal 8(5):225-233 (1995);	and cancers, such as, for
	Billiau et al., Ann NY Acad	example, leukemia, lymphoma,
	Sci 856:22-32 (1998); Boehm	melanoma, and prostate,
	et al., Annu Rev Immunol	breast, lung, colon, pancreatic,
	15:749-795 (1997), and	esophageal, stomach, brain,
	Rheumatology (Oxford)	liver and urinary cancer. Other
100	38(3):214-20 (1999), the	preferred indications include
	contents of each of which are	benign dysproliferative
	herein incorporated by	disorders and pre-neoplastic
	reference in its entirety.	conditions, such as, for
	Human T cells that may be	example, hyperplasia,
	used according to these assays	metaplasia, and/or dysplasia.
	may be isolated using	Preferred indications include
	techniques disclosed herein or	anemia, pancytopenia,
	otherwise known in the art.	leukopenia, thrombocytopenia,
	Human T cells are primary	Hodgkin's disease, acute
	human lymphocytes that	lymphocytic anemia (ALL),
	mature in the thymus and	plasmacytomas, multiple
	express a T Cell receptor and	myeloma, Burkitt's lymphoma,
	CD3, CD4, or CD8. These	arthritis, AIDS, granulomatous
	cells mediate humoral or cell-	disease, inflammatory bowel

disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described
mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in
	Activation of transcription through serum response element in immune cells (such as T-cells).
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	HELHD85
	173

below), immunodeficiencies (e.g., as described below),	immune response, and	suppressing a 1 cell-mediated immune response. Additional	highly preferred indications	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative
Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	85:6342-6346 (1988); and	Black et al., Virus Genes	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.									
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					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
				1	plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
		٠			disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
,•					disease as described below
					under "Infectious Disease").
	HELHL48	1122	CD152 in Human T		
			cells		
	HELHL48	1122	Activation or inhibition of	This reporter assay measures activation or inhibition of the	

,	transcription through NFKB response element in immune cells (such as basophils).	NFkB signaling pathway in Ku812 human basophil cell line. Assays for the activation or inhibition of transcription through the NFKB response element are well-known in the art and may be used or
		routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate
		immunomodulatory genes.  NFkB is important in the pathogenesis of asthma.  Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-
		response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol

216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Marone	et al, Int Arch Allergy Immunol 114(3):207-17 (1997), the contents of each of	which are herein incorporated by reference in its entirety. Cells were pretreated with SID	supernatants or controls for 15-18 hours, and then 10 ng/mL	the NFkB reporter. SEAP activity was measured after 48	hours. Basophils that may be	are publicly available (e.g.,	Exemplary human basophil	cell lines that may be used according to these assays	include Ku812, originally established from a patient with	chronic myelogenous	leukemia. It is an immature prebasophilic cell line that can	be induced to differentiate into	mature basophils. See, Kishi et	al., Leuk Res. 9:381-390	(1985); Blom et al., Eur J

				where the contents of each are	
				herein incorporated by	
				reference in its entirety.	
	HEMAM41	1123	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
175				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
***************************************				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
				Deregulated expression of IL-6	reducing) IL-6 production. A
				has been linked to autoimmune	highly preferrred indication is
				disease, plasmacytomas,	the stimulation or enhancement
				myelomas, and chronic	of mucosal immunity. Highly
				hyperproliferative diseases.	preferred indications include
				Assays for immunomodulatory	blood disorders (e.g., as
				and differentiation factor	described below under
4-4-4		,		proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
				expression level is strongly	"Cardiovascular Disorders"),
				regulated by cytokines, growth	and infection (e.g., as
				factors, and hormones are well	described below under
	*******			known in the art and may be	"Infectious Disease"). Highly
<del>* * *</del>				used or routinely modified to	preferred indications include
4.				assess the ability of	autoimmune diseases (e.g.,
				polypeptides of the invention	rheumatoid arthritis, systemic
				(including antibodies and	lupus erythematosis, multiple
				agonists or antagonists of the	sclerosis and/or as described
				invention) to mediate	below) and
				immunomodulation and	immunodeficiencies (e.g., as

				techniques disclosed herein or	pre-neoplastic conditions, such
				otherwise known in the art.	as, for example, hyperplasia,
				Human dendritic cells are	metaplasia, and/or dysplasia.
				antigen presenting cells in	Preferred indications include
				suspension culture, which,	anemia, pancytopenia,
				when activated by antigen	leukopenia, thrombocytopenia,
				and/or cytokines, initiate and	Hodgkin's disease, acute
				upregulate T cell proliferation	lymphocytic anemia (ALL),
				and functional activities.	multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
	HEMAM41	1123	Production of TNF	TNFa FMAT. Assays for	A highly preferred
175			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for
				macrophages, T cells,	inhibiting (e.g., decreasing)
				fibroblasts, smooth muscle,	TNF alpha production. An
				and other cell types that exert a	alternative highly preferred

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embodiment of the invention includes a method for	stimulating (e.g., increasing)	TNF alpha production.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neonlectic dispose
wide variety of inflammatory and evtotoxic effects on a	variety of cells are well known	in the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	mediate immunomodulation,	modulate inflammation and	cytotoxicity. Exemplary	assays that test for	immunomodulatory proteins	evaluate the production of	cytokines such as tumor	necrosis factor alpha (TNFa),	and the induction or inhibition	of an inflammatory or	cytotoxic response. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"I rimahoortoo: o motiool
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, , , , , , , , , , , , , , , , , , ,	approach" Chapter 6:138-160  (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890  (1198); Dahlen et al., J Immunol 160(7):3885-3593  Immunol 160(7):3885-3593  Immunol 160(7):3885-3593  Immunol 160(7):3885-3593  Immunol 162:2919-2925  Immunol 163:2919-2925  Immunol 163:2919  Immunol 163:2919-2925  Immunol 163:2919  Immunol	, , , , , , , , , , , , , , , , , , ,	, , , , , , , , , , , , , , , , , , ,	nia lymphoma	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	plasms and	cancers, such as, leukemia,	lymphoma, melanoma, glioma	(e.g., malignant glioma), solid	tumors, and prostate, breast,	pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	roliferative	disorders and pre-neoplastic	such as, for	/perplasia,	metaplasia, and/or dysplasia.	Preferred indications include	cytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	ıtropenia,	•
upproach" Chapter 6:138-16/2000); Verhasselt et al., Eur mmunol 28(11):3886-3890 (1198); Dahlen et al., J mmunol 160(7):3585-3593 (1998); Verhasselt et al., J mmunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1997); and nadelli et al., J Leukoc Biol 65:822-828 (1997); and hardelli et al., J Leukoc Biol 65:822-828 (1997); and hardelli et al., J Leukoc Biol 65:822-828 (1997); and hardelli et al., J Leukoc Biol 65:822-828 (1997); and dendritic cells that me be used according to these used to the to the total to the to	approach" Chapter 6:138-16i (2000); Verhasselt et al., Eur Immunol 28(11):3886-3890 (1198); Dahlen et al., J Immunol 160(7):3585-3593 (1998); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each which are herein incorporate by reference in its entirety. Human dendritic cells that m be used according to these assays may be isolated using techniques disclosed herein of otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferatio and functional activities.	approach" Chapter 6:138-16 (2000); Verhasselt et al., Eu Immunol 28(11):3886-3890 (1198); Dablen et al., J Immunol 160(7):385-3593 (1998); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each which are herein incorporate by reference in its entirety. Human dendritic cells that mbe used according to these assays may be isolated using techniques disclosed herein cotherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferatio and functional activities.	approach" Chapter 6:138-16 (2000), Verhasselt et al., Eu Immunol 28(11):386-3890 (1198), Dahlen et al., J Immunol 160(7):385-3593 (1998), Verhasselt et al., J Immunol 158:2919-2925 (1997), and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each which are herein incorporate by reference in its entirety. Human dendritic cells that me be used according to these assays may be isolated using techniques disclosed herein otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferatio and functional activities.				Disorders").	highly prefe	include neoplasms and	cancers, suc	lymphoma, 1	(e.g., malign	_	d   lung, colon, pancreatic,	esophageal,		preferred inc			conditions, such as, for	example, hyperplasia,	metaplasia,	Preferred in	anemia, pancytopenia,				plasmacyton	myeloma, B	arthritis, All	disease, infla	disease, neutropenia	Signature City of State Carticol
				unroach" Chanter 6:138-16	2000); Verhasselt et al., Eur	mmunol 28(11):3886-3890	1198); Dahlen et al., J	mmunol 160(7):3585-3593	1998); Verhasselt et al., J	mmunol 158:2919-2925	1997); and Nardelli et al., J	Jeukoc Biol 65:822-828	1999), the contents of each	which are herein incorporate	by reference in its entirety.	Tuman dendritic cells that m	be used according to these	issays may be isolated using	echniques disclosed herein c	otherwise known in the art.	<b>Human dendritic cells are</b>	antigen presenting cells in	suspension culture, which,	when activated by antigen	and/or cytokines, initiate and	apregulate T cell proliferatio	and functional activities.						

					reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease,
			,		cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below
	HEPAA46	1124	Activation of	Assays for the activation of	A preferred embodiment of
176			transcription	transcription through the	the invention includes a
			through serum response element in	Serum Response Element (SRE) are well-known in the	method for inhibiting (e.g., reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) INF alpha
				regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),
-				routinely modified to test SRE	Highly preferred indications
				activity of the polypeptides of	include autoimmune diseases
<del>y - i</del>				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,

		antagonists of the invention)	Crohn"s disease, multiple
		include assays disclosed in	sclerosis and/or as described
		Berger et al., Gene 66:1-10	below), immunodeficiencies
 		(1998); Cullen and Malm,	(e.g., as described below),
		Methods in Enzymol 216:362-	boosting a T cell-mediated
		368 (1992); Henthorn et al.,	immune response, and
		Proc Natl Acad Sci USA	suppressing a T cell-mediated
		85:6342-6346 (1988); and	immune response. Additional
		Black et al., Virus Genes	highly preferred indications
		12(2):105-117 (1997), the	include inflammation and
		content of each of which are	inflammatory disorders, and
		herein incorporated by	treating joint damage in
		reference in its entirety. T	patients with rheumatoid
		cells that may be used	arthritis. An additional highly
		according to these assays are	preferred indication is sepsis.
		publicly available (e.g.,	Highly preferred indications
		through the ATCC).	include neoplastic diseases
		Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
		may be used according to these	and/or as described below
		assays include the CTLL cell	under "Hyperproliferative
		line, which is an IL-2	Disorders"). Additionally,
 		dependent suspension culture	highly preferred indications
 		of T cells with cytotoxic	include neoplasms and
 		activity.	cancers; such as, for example,
 			leukemia, lymphoma,
			melanoma, glioma (e.g.,
 			malignant glioma), solid
 			tumors, and prostate, breast,
			lung, colon, pancreatic,
			esophageal, stomach, brain,
			liver and urinary cancer. Other

,				preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, leukopenia, thrombocytopenia, lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An
	·			is infection (e.g., an infectious disease as described below "t. f.
	HEPAA46	1124	IFNg in Human T- cell 2B9	under infectious Disease ).

	HEPAA46	1124	IL-2 in Human T-		
176			cell 2B9		
	HEPAB80	1125	Activation of	Kinase assay. Kinase assays,	A highly preferred
177			Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
			Signaling Pathway	assay, for ERK signal	includes a method for
				transduction that regulate cell	stimulating adipocyte
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment
				may be used or routinely	of the invention includes a
		_		modified to assess the ability	method for inhibiting
				of polypeptides of the	adipocyte proliferation. A
				invention (including antibodies	highly preferred embodiment
				and agonists or antagonists of	of the invention includes a
				the invention) to promote or	method for stimulating
				inhibit cell proliferation,	adipocyte differentiation. An
10				activation, and differentiation.	alternative highly preferred
				Exemplary assays for ERK	embodiment of the invention
				kinase activity that may be	includes a method for
				used or routinely modified to	inhibiting adipocyte
				test ERK kinase-induced	differentiation. A highly
				activity of polypeptides of the	preferred embodiment of the
				invention (including antibodies	invention includes a method
				and agonists or antagonists of	for stimulating (e.g.,
		-		the invention) include the	increasing) adipocyte
				assays disclosed in Forrer et	activation. An alternative
-				al., Biol Chem 379(8-9):1101-	highly preferred embodiment
				1110 (1998); Le Marchand-	of the invention includes a
	~			Brustel Y, Exp Clin	method for inhibiting the
				Endocrinol Diabetes	activation of (e.g., decreasing)
				107(2):126-132 (1999);	and/or inactivating adipocytes.
				Kyriakis JM, Biochem Soc	Highly preferred indications

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include endocrine disorders	(e.g., as described below under	"Endocrine Disorders").	Highly preferred indications	also include neoplastic	diseases (e.g., lipomas,	liposarcomas, and/or as	described below under	"Hyperproliferative			disorders (e.g., hypertension,	congestive heart failure, blood	vessel blockage, heart disease,	stroke, impotence and/or as	described below under	with "Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), neural	disorders (e.g., as described	below under "Neural Activity	and Neurological Diseases"),	and infection (e.g., as	described below under	"Infectious Disease").	A highly preferred indication	is diabetes mellitus.	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Mouse adipocyte cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC).	Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	conditions known in the art.						
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indication is a complication	associated with diabetes (e.g.,	diabelic relinopathy, diabelic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),
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disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as. for example. hyperplasia.	metaplasia, and/or dysplasia. A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal
	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta
	Regulation of viability and proliferation of pancreatic beta cells.
	1125
	HEPAB80
	177

				assays include HTTT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981	urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.
177	HEPAB80	1125	IL-6 in HUVEC		
178	HEQAK71	1126	Production of TNF alpha by dendritic cells	TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Highly preferred indications

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include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications
the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	mediate immunomodulation,	modulate inflammation and	cytotoxicity. Exemplary	assays that test for	immunomodulatory proteins	evaluate the production of	cytokines such as tumor	necrosis factor alpha (TNFa),	and the induction or inhibition	of an inflammatory or	cytotoxic response. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Verhasselt et al., Eur J	Immunol 28(11):3886-3890	(1198); Dahlen et al., J	Immunol 160(7):3585-3593
		<del></del> -																		-, "	·		-			-				,

include neoplasms and	cancers, such as, leukemia,	lymphoma, melanoma, glioma	(e.g., malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,		preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,
(1998); Verhasselt et al., J	Immunol 158:2919-2925	(1997); and Nardelli et al., J	Leukoc Biol 65:822-828	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which,	when activated by antigen	and/or cytokines, initiate and	upregulate T cell proliferation	and functional activities.												
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				Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	
621	HERAR44	1127	Activation of transcription	This reporter assay measures activation of the NFkB	Highly preferred indication includes allergy, asthma, and
			through NFKB response element in	signaling pathway in Ku812 human basophil cell line.	rhinitis. Additional highly preferred indications include
			immune cells (such as basophils).	Assays for the activation of transcription through the	infection (e.g., an infectious disease as described below
				NFKB response element are well-known in the art and may	under "Infections Disease"), and inflammation and
				be used or routinely modified	inflammatory disorders.
				to assess the ability of	Preferred indications include
				polypeptides of the invention	immunological and
				(including antibodies and agonists or antagonists of the	nempatopoietic disorders (e.g., as described below under
				invention) to regulate NFKB	"Immune Activity", and
				transcription factors and	"Blood-Related Disorders").
				modulate expression of	Preferred indications also
				immunomodulatory genes.	include autoimmune diseases
				Exemplary assays for	(e.g., rheumatoid arthritis,
	•			transcription through the	systemic lupus erythematosis,
				NFKB response element that	multiple sclerosis and/or as
				may be used or rountinely	described below) and
				modified to test NFKB-	immunodeficiencies (e.g., as
				response element activity of	described below). Preferred
				polypeptides of the invention	indications also include
		-		(including antibodies and	neoplastic diseases (e.g.,
				agonists or antagonists of the	leukemia, lymphoma,
				invention) include assays	melanoma, and/or as described

				disclosed in Berger et al., Gene	below under
				66:1-10 (1998); Cullen and	"Hyperproliferative
				Malm, Methods in Enzymol	Disorders"). Preferred
				216:362-368 (1992); Henthorn	indications include neoplasms
	,			et al., Proc Natl Acad Sci USA	and cancer, such as, for
				85:6342-6346 (1988); Marone	example, leukemia, lymphoma,
				et al, Int Arch Allergy	melanoma, and prostate,
				Immunol 114(3):207-17	breast, lung, colon, pancreatic,
				(1997), the contents of each of	esophageal, stomach, brain,
				which are herein incorporated	liver, urinary tract cancers and
				by reference in its entirety.	as described below under
				Basophils that may be used	"Hyperproliferative
				according to these assays are	Disorders".
				publicly available (e.g.,	
				through the ATCC).	
10				Exemplary human basophil	
				cell lines that may be used	
				according to these assays	
				include Ku812, originally	
				established from a patient with	
				chronic myelogenous	
				leukemia. It is an immature	
				prebasophilic cell line that can	
				be induced to differentiate into	
				mature basophils.	
	HERAR44	1127	Production of	Assays for measuring	Preferred embodiments of the
179			ICAM-1	expression of ICAM-1 are	invention include using
				well-known in the art and may	polypeptides of the invention
<del>.</del> .				be used or routinely modified	(or antibodies, agonists, or
······································				to assess the ability of	antagonists thereof) in
				polypeptides of the invention	detection, diagnosis,

				(including antibodies and	prevention, and/or treatment of
				agonists or antagonists of the	Inflammation, Vascular
				invention) to regulate ICAM-1	Disease, Athereosclerosis,
				expression. Exemplary assays	Restenosis, and Stroke
				that may be used or routinely	
				modified to measure ICAM-1	
				expression include assays	
				disclosed in: Takacs P, et al,	
				FASEB J, 15(2):279-281	
				(2001); and, Miyamoto K, et	
				al., Am J Pathol, 156(5):1733-	
				1739 (2000), the contents of	
				each of which is herein	
				incorporated by reference in its	
				entirety. Cells that may be	
				used according to these assays	
				are publicly available (e.g.,	
				through the ATCC) and/or	
				may be routinely generated.	
				Exemplary cells that may be	
				used according to these assays	
				include microvascular	
			3	endothelial cells (MVEC).	
	HESAJ10	1128	Regulation of	Caspase Apoptosis. Assays for	Preferred embodiments of the
180			apoptosis of	caspase apoptosis are well	invention include using
			immune cells (such	known in the art and may be	polypeptides of the invention
			as mast cells).	used or routinely modified to	(or antibodies, agonists, or
				assess the ability of	antagonists thereof) in
				polypeptides of the invention	detection, diagnosis,
				(including antibodies and	prevention, and/or treatment of
				agonists or antagonists of the	asthma, allergy,

e hypersensitivity and	in inflammation.		st		nc			ra			on				9				he	ies	ıf.		Α,			dx			for	
invention) to regulate caspase	protease-mediated apoptosis in	immune cells (such as, for	example, in mast cells). Mast	cells are found in connective	and mucosal tissues throughout	the body, and their activation	via immunoglobulin E -	antigen, promoted by T helper	cell type 2 cytokines, is an	important component of	allergic disease. Dysregulation	of mast cell apoptosis may	play a role in allergic disease	and mast cell tumor survival.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	capase apoptosis activity	induced by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in: Masuda A,	et al., J Biol Chem,	276(28):26107-26113 (2001);	Yeatman CF 2nd, et al., J Exp	Med, 192(8):1093-1103	(2000);Lee et al., FEBS Lett	485(2-3): 122-126 (2000); Nor	et al., J Vasc Res 37(3): 209-
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																-					-									

218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.	This reporter assay measures activation or inhibition of the NFkB signaling pathway in Ku812 human basophil cell line. Assays for the activation or inhibition of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate
	Activation or inhibition of transcription through NFKB response element in immune cells (such as basophils).
	1129
	HETAB45
	181

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expression of	immunomodulatory genes.	NFkB is important in the	pathogenesis of asthma.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Marone	et al, Int Arch Allergy	Immunol 114(3):207-17	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Cells were pretreated with SID	supernatants or controls for 15-	18 hours, and then 10 ng/mL	of TNF was added to stimulate	the NFkB reporter. SEAP	activity was measured after 48
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	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Cancer, Autoimmunity, Allergy and Asthma
hours. Basophils that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary human basophil cell lines that may be used according to these assays include Ku812, originally established from a patient with chronic myelogenous leukemia. It is an immature prebasophilic cell line that can be induced to differentiate into mature basophils. See, Kishi et al., Leuk Res. 9:381-390 (1985); Blom et al., Eur J Immunol. 22:2025-32 (1992), where the contents of each are herein incorporated by reference in its entirety.	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and
	Activation of transcription through NFKB response element in immune cells (such as B-cells).
-	1129
	HETAB45
	181

modulate expression of immunomodulatory genes.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in: Gri G, et al., Biol	Chem, 273(11):6431-6438	(1998); Pyatt DW, et al., Cell	Biol Toxicol 2000;16(1):41-51	(2000); Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Valle	Blazquez et al, Immunology	90(3):455-460 (1997);	Aramburau et al., J Exp Med	82(3):801-810 (1995); and	Fraser et al., 29(3):838-844	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Immune cells that may be used
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t esse	Preferred embodiments of the invention include using polypeptides of the invention of or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, sys Restenosis, and Stroke its
according to these assays are publicly available (e.g., through the ATCC).  Exemplary immune cells that may be used according to these assays include the Reh B-cell line.	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or
	Production of ICAM-1
	1130
	HETBR16
	182

				may be routinely generated	
				Exemplary cells that may be	
				used according to these assays include microvascular endothelial cells (MVEC).	
182	HETBR16	1130	SEAP in OE-21		
	HETLM70	1131	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
183				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
				Deregulated expression of IL-6	reducing) IL-6 production. A
				has been linked to autoimmune	highly preferrred indication is
				disease, plasmacytomas,	the stimulation or enhancement
				myelomas, and chronic	of mucosal immunity. Highly
				hyperproliferative diseases.	preferred indications include
	-			Assays for immunomodulatory	blood disorders (e.g., as
				and differentiation factor	described below under
				proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
				expression level is strongly	"Cardiovascular Disorders"),
				regulated by cytokines, growth	and infection (e.g., as
				factors, and hormones are well	described below under
				known in the art and may be	"Infectious Disease"). Highly
				used or routinely modified to	preferred indications include
				assess the ability of	autoimmune diseases (e.g.,
				polypeptides of the invention	rheumatoid arthritis, systemic

				by reference in its entirety.	stomach, brain, liver and
				Human dendritic cells that may	urinary cancer. Other preferred
				be used according to these	indications include benign
				assays may be isolated using	dysproliferative disorders and
				techniques disclosed herein or	pre-neoplastic conditions, such
				otherwise known in the art.	as, for example, hyperplasia,
				Human dendritic cells are	metaplasia, and/or dysplasia.
				antigen presenting cells in	Preferred indications include
				suspension culture, which,	anemia, pancytopenia,
				when activated by antigen	leukopenia, thrombocytopenia,
				and/or cytokines, initiate and	Hodgkin's disease, acute
				upregulate T cell proliferation	lymphocytic anemia (ALL),
				and functional activities.	multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
		-			sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
	,	:			Disease").
183	HETLM70	1131	Production of MIP1alpha	MIP-1alpha FMAT. Assays for immunomodulatory	A highly preferred embodiment of the invention

proteins produced by activated dendritic cells that upregulate	includes a method for stimulating MIP1a production.
monocyte/macrophage and 1 cell chemotaxis are well	An alternative highly preferred embodiment of the invention
known in the art and may be	includes a method for
used or routinely modified to	inhibiting (e.g., reducing)
polypeptides of the invention	is
(including antibodies and	infection (e.g., an infectious
agonists or antagonists of the	disease as described below
invention) to mediate	under "Infectious Disease").
immunomodulation, modulate	Preferred indications include
chemotaxis, and modulate T	blood disorders (e.g., as
cell differentiation. Exemplary	
assays that test for	"Immune Activity", "Blood-
immunomodulatory proteins	Related Disorders", and/or
evaluate the production of	"Cardiovascular Disorders").
chemokines, such as	Highly preferred indications
macrophage inflammatory	include autoimmune diseases
protein 1 alpha (MIP-1a), and	(e.g., rheumatoid arthritis,
the activation of	
monocytes/macrophages and T	
cells. Such assays that may be	
used or routinely modified to	immunodeficiencies (e.g., as
test immunomodulatory and	described below). Additional
chemotaxis activity of	highly preferred indications
polypeptides of the invention	include inflammation and
(including antibodies and	inflammatory disorders.
agonists or antagonists of the	Preferred indications also
invention) include assays	include anemia, pancytopenia,
disclosed in Miraglia et al., J	leukopenia, thrombocytopenia,

Hodgkin's disease, acute	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes		meningitis, Lyme Disease,	asthma, and allergy.	y Preferred indications also	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for
Biomolecular Screening 4:193-	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Satthaporn and	Eremin, J R Coll Surg Ednb	(45(1):9-19 (2001); Drakes et	al., Transp Immunol 8(1):17-	29 (2000); Verhasselt et al., J	Immunol 158:2919-2925	(1997); and Nardelli et al., J	Leukoc Biol 65:822-828	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which,	when activated by antigen	and/or cytokines, initiate and	upregulate T cell proliferation	and functional activities.				
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example, hyperplasia, metaplasia, and/or dysplasia.		ory proteins embodiment of the invention vated includes a method for	 uscle,		nflammatory embodiment of the invention	fects on a   includes a method for	re well known   stimulating (e.g., increasing)	be used or TNF alpha production.				gonists or   "Immune Activity", "Blood-		modulation,   "Cardiovascular Disorders"),	mation and Highly preferred indications	emplary   include autoimmune diseases	or (e.g., rheumatoid arthritis,	ory proteins   systemic lupus erythematosis,	duction of   Crohn's disease, multiple	s tumor sclerosis and/or as described	lpha (TNFa),   below), immunodeficiencies				be used or   suppressing a T cell-mediated	and to test   immine response Additional
	r.	cells produced by activated	fibroblasts, smooth muscle,	and other cell types that exert a	wide variety of inflammatory	and cytotoxic effects on a	variety of cells are well known	in the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	mediate immunomodulation,	modulate inflammation and	cytotoxicity. Exemplary	assays that test for	immunomodulatory proteins	evaluate the production of	cytokines such as tumor	necrosis factor alpha (TNFa),	and the induction or inhibition	of an inflammatory or	cytotoxic response. Such	assays that may be used or	routinely modified to test
	HETLM70 1131																									
	103	103																								

	polypeptides of the invention	include inflammation and
	(including antibodies and	inflammatory disorders, and
	agonists or antagonists of the	treating joint damage in
	invention) include assays	patients with rheumatoid
	disclosed in Miraglia et al., J	arthritis. An additional highly
	Biomolecular Screening 4:193-	preferred indication is sepsis.
	204(1999); Rowland et al.,	Highly preferred indications
	"Lymphocytes: a practical	include neoplastic diseases
	approach" Chapter 6:138-160	(e.g., leukemia, lymphoma,
	(2000); Verhasselt et al., Eur J	and/or as described below
	Immunol 28(11):3886-3890	under "Hyperproliferative
	(1198); Dahlen et al., J	Disorders"). Additionally,
	Immunol 160(7):3585-3593	highly preferred indications
	(1998); Verhasselt et al., J	include neoplasms and
	Immunol 158:2919-2925	cancers, such as, leukemia,
	(1997); and Nardelli et al., J	lymphoma, melanoma, glioma
	Leukoc Biol 65:822-828	(e.g., malignant glioma), solid
	(1999), the contents of each of	tumors, and prostate, breast,
	which are herein incorporated	lung, colon, pancreatic,
	by reference in its entirety.	esophageal, stomach, brain,
	Human dendritic cells that may	liver and urinary cancer. Other
	be used according to these	preferred indications include
	assays may be isolated using	benign dysproliferative
	techniques disclosed herein or	disorders and pre-neoplastic
	otherwise known in the art.	conditions, such as, for
	Human dendritic cells are	example, hyperplasia,
	antigen presenting cells in	metaplasia, and/or dysplasia.
	suspension culture, which,	Preferred indications include
	when activated by antigen	anemia, pancytopenia,
	and/or cytokines, initiate and	leukopenia, thrombocytopenia,
	upregulate T cell proliferation	Hodgkin's disease, acute

				and functional activities.	lymphocytic anemia (ALL),
					plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below
183	HETLM70	1131	SEAP in HIB/CRE		
184	HFABG18	1132	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment

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of the invention includes a	method for stimulating	adipocyte differentiation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting adipocyte	differentiation. A highly	preferred embodiment of the	invention includes a method	for stimulating (e.g.,	increasing) adipocyte	activation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting the	activation of (e.g., decreasing)	and/or inactivating adipocytes.	Highly preferred indications	include endocrine disorders	(e.g., as described below under	"Endocrine Disorders").	Highly preferred indications	also include neoplastic	diseases (e.g., lipomas,	liposarcomas, and/or as	described below under	"Hyperproliferative	Disorders"). Preferred	indications include blood	disorders (e.g. hynertension
and agonists or antagonists of	the invention) to promote or	inhibit cell proliferation,	activation, and differentiation.	Exemplary assays for ERK	kinase activity that may be	used or routinely modified to	test ERK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Le Marchand-	Brustel Y, Exp Clin	Endocrinol Diabetes	107(2):126-132 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Mouse adipocyte cells that	may be used according to these	assays are publicly available	(P a throngh the ATCC)
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congestive heart failure, blood	vessel blockage, heart disease,	stroke, impotence and/or as	described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), neural	disorders (e.g., as described	below under "Neural Activity	and Neurological Diseases"),	and infection (e.g., as	described below under	"Infectious Disease").	A highly preferred indication	is diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic
Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	conditions known in the art.																		
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		neuropathy), blood vessel
		blockage, heart disease, stroke,
		impotence (e.g., due to diabetic
 		neuropathy or blood vessel
		blockage), seizures, mental
		confusion, drowsiness,
		nonketotic hyperglycemic-
 		hyperosmolar coma,
		cardiovascular disease (e.g.,
		heart disease, atherosclerosis,
 		microvascular disease,
		hypertension, stroke, and other
 		diseases and disorders as
 		described in the
		"Cardiovascular Disorders"
 		section below), dyslipidemia,
		endocrine disorders (as
		described in the "Endocrine
 		Disorders" section below),
 		neuropathy, vision impairment
		(e.g., diabetic retinopathy and
 		blindness), ulcers and impaired
 	-	wound healing, infection (e.g.,
 		infectious diseases and
	·	disorders as described in the
		"Infectious Diseases" section
		below (particularly of the
 		urinary tract and skin). An
		additional highly preferred
		indication is obesity and/or
		complications associated with

obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional	red in asscrance.	musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein.  Additional highly preferred	indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis,	disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as,	lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer.

					Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
184	HFABG18	1132	Protection from Endothelial Cell Apoptosis.	Caspase Apoptosis Rescue. Assays for caspase apoptosis rescue are well known in the art and may be used or routinely modified to assess the ability of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to inhibit caspase proteasemediated apoptosis.  Exemplary assays for caspase apoptosis that may be used or routinely modified to test caspase apoptosis rescue of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Romeo et al.,	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for inhibiting endothelial cell stimulating endothelial cell stimulating endothelial cell stimulating endothelial cell stimulating endothelial cell
				(2000), Messiller et al., DI 3 Pharmacol 127(7): 1633-1640	grown. An ancinative inginy preferred embodiment of the

invention includes a method	for inhibiting endothelial cell	growth. A highly preferred	embodiment of the invention	includes a method for	stimulating apoptosis of	endothelial cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under
(1999); and J Atheroscler	Thromb 3(2): 75-80 (1996);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through commercial sources).	Exemplary endothelial cells	that may be used according to	these assays include bovine	aortic endothelial cells	(bAEC), which are an example	of endothelial cells which line	blood vessels and are involved	in functions that include, but	are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.										
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		i     	"Hyperproliferative
		in the second	Disorders'), and disorders of
			the cardiovascular system
	4		(e.g., heart disease, congestive
			heart failure, hypertension,
			aortic stenosis,
	-	-	cardiomyopathy, valvular
			regurgitation, left ventricular
			dysfunction, atherosclerosis
			and atherosclerotic vascular
			disease, diabetic nephropathy,
	-		intracardiac shunt, cardiac
			hypertrophy, myocardial
			infarction, chronic
			hemodynamic overload, and/or
			as described below under
			"Cardiovascular Disorders").
			Highly preferred indications
			include cardiovascular,
			endothelial and/or angiogenic
			disorders (e.g., systemic
			disorders that affect vessels
			such as diabetes mellitus, as
			well as diseases of the vessels
			themselves, such as of the
			arteries, capillaries, veins
			and/or lymphatics). Highly
			preferred are indications that
			stimulate angiogenesis and/or
			cardiovascularization. Highly
_			nreferred are indications that

inhibit angiogenesis and/or cardiovascularization. Highly preferred indications include antiangiogenic activity to treat solid tumors,	sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi's sarcoma,	hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma,	angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also	prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign	dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications

also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or

other retinopathies, thrombotic and coagulative disorders,	vascularitis, lymph angiogenesis, sexual disorders,	age-related macular	prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	preferred indications include	inflammation and	inflammatory disorders (such	as acute and chronic
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					inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
	HFABG18	1132	Production of	IFNgamma FMAT. IFNg plays	A highly preferred
184			IFNgamma using a	a central role in the immune	embodiment of the invention
			T cells	system and is considered to be	includes a method for
				a proinflammatory cytokine.	stimulating the production of
				IFNg promotes TH1 and	IFNg. An alternative highly
	a			inhibits TH2 differentiation;	preferred embodiment of the
				promotes IgG2a and inhibits	invention includes a method
		•		IgE secretion; induces	for inhibiting the production of
				macrophage activation; and	IFNg. Highly preferred
				increases MHC expression.	indications include blood
				Assays for immunomodulatory	disorders (e.g., as described
	<del></del>			proteins produced by T cells	below under "Immune
				and NK cells that regulate a	Activity", "Blood-Related
				variety of inflammatory	Disorders", and/or
				activities and inhibit TH2	"Cardiovascular Disorders"),
				helper cell functions are well	and infection (e.g., viral
				known in the art and may be	infections, tuberculosis,
				used or routinely modified to	infections associated with
		_		assess the ability of	chronic granulomatosus
,	-			polypeptides of the invention	disease and malignant
		í		(including antibodies and	osteoporosis, and/or as
				agonists or antagonists of the	described below under
				invention) to mediate	"Infectious Disease"). Highly
				immunomodulation, regulate	preferred indications include
				inflammatory activities,	autoimmune disease (e.g.,
				modulate TH2 helper cell	rheumatoid arthritis, systemic
				function, and/or mediate	lupus erythematosis, multiple

humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as Interferon gamma (FNg), and the activation of Teells. Such a sasays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention of (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193- below under "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., JClin Listane et al., Ann NY Acad Sci 856:22-32 (1997), and Rheumatology (Oxford) preferred indications include neoplasmis include neoplasmis approach" Chapter 6:138-160 (2000); Gonzalez et al., JClin Listane et al., Ann NY Acad Sci 856:22-32 (1997), and Rheumatology (Oxford) (oxford) preferred indications include neoplasmis include neoplasmis approach" Chapter 6:138-160 (2000); Gonzalez et al., JClin Listane et al., Ann NY Acad Sci 856:22-32 (1997), and Rheumatology (Oxford) (oxford) preferred indications include contents of each of which are disorders and prostate chemin incorporated by	says the say
humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as Interferon gamma (IFNg), and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by	humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as Interferon gamma (IFNg), and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193–204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Ann Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by

HFABG18	1132	TNFa in Human T-	used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cellmediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	example, hyperphasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
HFABG18	1132	cell 2B9 SEAP in		
HFAMB72	1133	Activation of JNK Signaling Pathway in immune cells (such as eosinophils).	Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of	Highly preferred indications include asthma, allergy, hypersensitivity reactions, inflammation, and inflammatory disorders.  Additional highly preferred indications include immune

polypeptides of the invention	and hematopoietic disorders
(including antibodies and	(e.g., as described below under
agonists or antagonists of the	"Immune Activity", and
invention) to promote or	"Blood-Related Disorders"),
inhibit cell proliferation,	autoimmune diseases (e.g.,
 activation, and apoptosis.	rheumatoid arthritis, systemic
Exemplary assays for JNK	lupus erythematosis, Crohn"s
 kinase activity that may be	disease, multiple sclerosis
used or routinely modified to	and/or as described below),
test JNK kinase-induced	immunodeficiencies (e.g., as
activity of polypeptides of the	described below). Highly
invention (including antibodies	preferred indications also
 and agonists or antagonists of	include boosting or inhibiting
 the invention) include the	immune cell proliferation.
assays disclosed in Forrer et	Preferred indications include
al., Biol Chem 379(8-9):1101-	neoplastic diseases (e.g.,
1110 (1998); Gupta et al., Exp	leukemia, lymphoma, and/or as
Cell Res 247(2): 495-504	described below under
 (1999); Kyriakis JM, Biochem	"Hyperproliferative
Soc Symp 64:29-48 (1999);	Disorders"). Highly preferred
Chang and Karin, Nature	indications include boosting an
410(6824):37-40 (2001); and	eosinophil-mediated immune
Cobb MH, Prog Biophys Mol	response, and suppressing an
Biol 71(3-4):479-500 (1999);	eosinophil-mediated immune
the contents of each of which	response.
are herein incorporated by	
reference in its entirety.	
Exemplary cells that may be	,
used according to these assays	
include eosinophils.	
Eosinophils are important in	

the late stage of allergic reactions; they are recruited to	tissues and mediate the	inflammatory response of late	stage allergic reaction.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and	activation of c-Jun NH2-	terminal kinase and p38	mitogen-activated protein	kinase in human eosinophils"	Clin Exp Immunol;	Oct;122(1):20-7 (2000);	Hebestreit H, et al.,	"Disruption of fas receptor	signaling by nitric oxide in	eosinophils" J Exp Med; Feb	2;187(3):415-25 (1998); J	Allergy Clin Immunol 1999
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				Sep;104(3 Pt 1):565-74; and,	
				Sousa AR, et al., "In vivo	
				resistance to corticosteroids in	
				bronchial asthma is associated	
				with enhanced	
				phosyphorylation of JUN N-	•
				terminal kinase and failure of	
				prednisolone to inhibit JUN N-	
				terminal kinase	
				phosphorylation" J Allergy	
				Clin Immunol; Sep;104(3 Pt	
				1):565-74 (1999); the contents	
				of each of which are herein	
				incorporated by reference in its	
		400		entirety.	
	HFAMH77	1134	Activation of	Assays for the activation of	A preferred embodiment of
186			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
		_		the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
		_		regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),

			routinely modified to test SRE	Highly preferred indications
			activity of the polypeptides of	include autoimmune diseases
			the invention (including	(e.g., rheumatoid arthritis,
			antibodies and agonists or	systemic lupus erythematosis,
			antagonists of the invention)	Crohn"s disease, multiple
			include assays disclosed in	sclerosis and/or as described
			Berger et al., Gene 66:1-10	below), immunodeficiencies
			(1998); Cullen and Malm,	(e.g., as described below),
			Methods in Enzymol 216:362-	boosting a T cell-mediated
			368 (1992); Henthorn et al.,	immune response, and
			Proc Natl Acad Sci USA	suppressing a T cell-mediated
			85:6342-6346 (1988); and	immune response. Additional
			Black et al., Virus Genes	highly preferred indications
			12(2):105-117 (1997), the	include inflammation and
			content of each of which are	inflammatory disorders, and
•			herein incorporated by	treating joint damage in
			reference in its entirety. T	patients with rheumatoid
			cells that may be used	arthritis. An additional highly
			according to these assays are	preferred indication is sepsis.
			publicly available (e.g.,	Highly preferred indications
			through the ATCC).	include neoplastic diseases
	•		Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
_			may be used according to these	and/or as described below
			assays include the CTLL cell	under "Hyperproliferative
			line, which is an IL-2	Disorders"). Additionally,
		•	dependent suspension culture	highly preferred indications
			of T cells with cytotoxic	include neoplasms and
			activity.	cancers, such as, for example,
				leukemia, lymphoma,
				melanoma, glioma (e.g.,
				malignant glioma), solid

tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other	preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include	anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted	organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious

disease as described below under "Infectious Disease").	<u> </u>	embodiment of the invention includes a method for	stimulating the production of	IFNg. An alternative highly	preferred embodiment of the	invention includes a method	for inhibiting the production of	IFNg. Highly preferred		disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or as	described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune disease (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiency
	IFNgamma FMAT. IFNg plays	system and is considered to be	a proinflammatory cytokine.	IFNg promotes TH1 and	inhibits TH2 differentiation;	promotes IgG2a and inhibits	IgE secretion; induces	macrophage activation; and	increases MHC expression.	Assays for immunomodulatory	proteins produced by T cells	and NK cells that regulate a	variety of inflammatory	activities and inhibit TH2	helper cell functions are well	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, regulate	inflammatory activities,	modulate TH2 helper cell	function, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays
1	Production of	IFINGALILITA USING A   T cells																										
	1134																											i
	HFAMH77		-																									
	186	201																										

		that test for		(e.g., as described below),
		immunomodulatory proteins	tory proteins	boosting a T cell-mediated
		evaluate the production of	duction of	immune response, and
		cytokines, such as Interferon	as Interferon	suppressing a T cell-mediated
		gamma (IFNg), and the	and the	immune response. Additional
		activation of T cells. Such	cells. Such	highly preferred indications
		assays that may be used or	be used or	include inflammation and
-		routinely modified to test	ied to test	inflammatory disorders.
		immunomodula	immunomodulatory activity of	Additional preferred
		polypeptides of the invention	the invention	indications include idiopathic
		(including antibodies and	odies and	pulmonary fibrosis. Highly
		agonists or antagonists of the	gonists of the	preferred indications include
		invention) include the assays	de the assays	neoplastic diseases (e.g.,
		disclosed in Miraglia et al., J	raglia et al., J	leukemia, lymphoma,
		Biomolecular S	Biomolecular Screening 4:193-	melanoma, and/or as described
		204 (1999); Rowland et al.,	wland et al.,	below under
		"Lymphocytes: a practical	a practical	"Hyperproliferative
		approach" Chapter 6:138-160	ter 6:138-160	Disorders"). Highly preferred
		(2000); Gonzalez et al., J Clin	ez et al., J Clin	indications include neoplasms
	_	Lab Anal 8(5):2	Lab Anal 8(5):225-233 (1995);	and cancers, such as, for
		Billiau et al., Ann NY Acad	nn NY Acad	example, leukemia, lymphoma,
		Sci 856:22-32 (1998); Boehm	1998); Boehm	melanoma, and prostate,
		et al., Annu Rev Immunol	/ Immunol	breast, lung, colon, pancreatic,
		15:749-795 (1997), and	97), and	esophageal, stomach, brain,
-		Rheumatology (Oxford)	(Oxford)	liver and urinary cancer. Other
		38(3):214-20 (1999), the	999), the	preferred indications include
		contents of each of which are	of which are	benign dysproliferative
		herein incorporated by	ated by	disorders and pre-neoplastic
		reference in its entirety.	entirety.	conditions, such as, for
		Human T cells that may be	that may be	example, hyperplasia,
		used according to these assays		metaplasia, and/or dysplasia.

Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	
may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cellmediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	RANTES FMAT. Assays for immunomodulatory proteins that induce chemotaxis of T cells, monocytes, and eosinophils are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and/or
	Production of RANTES in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
	1134
	HFAMH77
1225	186

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mediate humoral or cell-	mediated immunity.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as RANTES,	and the induction of	chemotactic responses in	immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Cocchi et al., Science	270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp	Immunol 101(3):398-407	(1995), the contents of each of	which are herein incorporated	by reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,
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	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing)  TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing)  TNF alpha production.  Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases
through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.	TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate inflammation and cytotoxicity. Exemplary
	Production of TNF alpha by dendritic cells
	1135
	HFCCQ50
	187

	proteins systemic lupus erythematosis,				inhibition (e.g., as described below),	-	•	sed or suppressing a T cell-mediated		activity of   highly preferred indications	invention include inflammation and	s and inflammatory disorders, and	sts of the   treating joint damage in	ssays patients with rheumatoid		ning 4:193- preferred indication is sepsis.	t et al., Highly preferred indications	actical include neoplastic diseases	5:138-160 (e.g., leukemia, lymphoma,	t al., Eur J   and/or as described below	<u> </u>	., J   Disorders"). Additionally,	S5-3593 highly preferred indications	et al., J include neoplasms and	cancers, such as, leukemia,		-828 (e.g., malignant glioma), solid		corporated   lung, colon, pancreatic,	
assays that test for	immunomodulatory proteins	evaluate the production of	cytokines such as tumor	necrosis factor alpha (TNFa),	and the induction or inhibition	of an inflammatory or	cytotoxic response. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Verhasselt et al., Eur J	Immunol 28(11):3886-3890	(1198); Dahlen et al., J	Immunol 160(7):3585-3593	(1998); Verhasselt et al., J	Immunol 158:2919-2925	(1997); and Nardelli et al., J	Leukoc Biol 65:822-828	(1999), the contents of each of	which are herein incorporated	hy reference in its entirety
	-						_									-		-												

			may	liver and urinary cancer. Other
			be used according to these	preferred indications include benian dysproliferative
			techniques disclosed herein or	disorders and pre-neoplastic
			otherwise known in the art.	conditions, such as, for
			Human dendritic cells are	example, hyperplasia,
			antigen presenting cells in	metaplasia, and/or dysplasia.
			suspension culture, which,	Preferred indications include
			when activated by antigen	anemia, pancytopenia,
			and/or cytokines, initiate and	leukopenia, thrombocytopenia,
			upregulate T cell proliferation	Hodgkin's disease, acute
			and functional activities.	lymphocytic anemia (ALL),
				plasmacytomas, multiple
-				myeloma, Burkitt's lymphoma,
				arthritis, AIDS, granulomatous
				disease, inflammatory bowel
				disease, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
	_			meningitis, Lyme Disease,
				cardiac reperfusion injury, and
				asthma and allergy. An
				additional preferred indication
				is infection (e.g., an infectious
				disease as described below
				under "Infectious Disease").
HFCCQ50	1135	Glucose Production		

HFCCQ50	0 1135	in H4IIE Production of IL-4	IL-4 FMAT. Assays for	A highly preferred
,			immunomodulatory proteins	embodiment of the invention
			secreted by 1H2 cells that	includes a memou for stimulating (e.g., increasing)
			macrophages and mast cells	IL-4 production. An alternative
<del></del>	<del>,</del>		and promote polarization of	highly preferred embodiment
			CD4+ cells into TH2 cells are	of the invention includes a
			well known in the art and may	method for inhibiting (e.g.,
			be used or routinely modified	reducing) IL-4 production.
			to assess the ability of	A highly preferred indication
			polypeptides of the invention	includes asthma. A highly
			(including antibodies and	preferred indication includes
			agonists or antagonists of the	allergy. A highly preferred
			invention) to mediate	indication includes rhinitis.
			immunomodulation, stimulate	Additional highly preferred
			immune cells, modulate	indications include
		•	immune cell polarization,	inflammation and
			and/or mediate humoral or	inflammatory disorders.
_			cell-mediated immunity.	Highly preferred indications
			Exemplary assays that test for	include neoplastic diseases
			immunomodulatory proteins	(e.g., leukemia, lymphoma,
			evaluate the production of	melanoma, and/or as described
			cytokines, such as IL-4, and	below under
			the stimulation of immune	"Hyperproliferative
			cells, such as B cells, T cells,	Disorders"). Preferred
			macrophages and mast cells.	indications include neoplasms
			Such assays that may be used	and cancers, such as, for
			or routinely modified to test	example, leukemia, lymphoma,
			immunomodulatory activity of	melanoma, and prostate,
			nolypeptides of the invention	breast, lung, colon, pancreatic,

geonists or anagonists of the irwention include the assays of the irwention) include the assays of disclosed in Miraglia et al., J. Biomolecular Screening 4:193 – denign dysproliferative Biomolecular Screening 4:194 – conditions, such as, for example, hyperplasia, approach" Chapter 6:138-160 metaplasia, and/or dysplasia, (2000) Gonzalez et al., Nel Immunol 1(3):257 – Related Disorders" and/or 26: (2000), and van der Graaff (2000), convalez et al., Net Immunol 1(3):257 – Cardiovascular Disorders". St. (2000), and van der Graaff (
(including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193–204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., 1 Clin Lab Anal 8(5):277-283 (1194); Yssel et al., Res Immunol 144(8):610-616 (1993); Bagley et al., Nat Immunol 1(3):257–261 (2000); and van der Graaff et al., Rheumatology (Oxford) 38(3):214-220 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may

disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include immunological and hematopoietic disorders (e.g., as described below under "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as described below). An
be preactivated to enhance responsiveness to immunomodulatory factors.	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-
	Activation of transcription through NFKB response element in immune cells (such as the Jurkat human T cell line).
	1135
	HFCCQ50
	187

additional highly preferred indication is infection (e.g., AIDS, and/or an infectious disease as described below		(e.g., melanoma, leukemia, lymphoma, and/or as described below under		indications include neoplasms	and cancers, such	as,melanoma, renal cell carcinoma. leukemia.			esophageal, stomach, brain,	liver and urinary cancer. Other preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,			include anemia, pancytopenia,	leukopenia, thrombocytopenia,	, Hodgkin's disease, acute	lymphocytic anemia (ALL),
response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the	invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and	Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al Proc Natl Acad Sci USA	85:6342-6346 (1988); Valle	90(3):455-460 (1997);	Aramburau et al., J Exp Med	82(3):801-810 (1995); and Fraser et al., 29(3):838-844	(1999), the contents of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used   according to these assays are	publicly available (e.g.,	through the ATCC). T cells	that may be used according to	these assays are publicly	available (e.g., through the	ATCC). Exemplary human T	cells that may be used	according to these assays	include the JURKAT cell line,	which is a suspension culture
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			of leukemia cells that produce IL-2 when stimulated.	plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted
<b>Н</b> FCСQ50	1135	Activation of transcription through GAS response element in immune cells (such as monocytes).	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Infection, Cancer, Hypersensitivity, and Atherosclerosis.

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routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays	disclosed in: Gustafson KS, et al., J Biol Chem, 271(33):20035-20046 (1996); Eilers A, et al., Immunobiology, 193(2-4):328-333 (1995); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol	216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety.  Exemplary immune cells that may be used according to these assays are publicly available	(e.g., through the ATCC).  Exemplary immune cells that may be used according to these assays include the U937 cell

				line, which is a monocytic cell	
				line.	Public and Control of the Control of
	HFCEW05	1136	Production of	Assays for measuring	Highly preferred indications
188			VCAM in	expression of VCAM are well-	include inflammation (acute
			endothelial cells	known in the art and may be	and chronic), restnosis,
			(such as human	used or routinely modified to	atherosclerosis, asthma and
			umbilical vein	assess the ability of	allergy. Highly preferred
		•	endothelial cells	polypeptides of the invention	indications include
			(HUVEC))	(including antibodies and	inflammation and
				agonists or antagonists of the	inflammatory disorders,
				invention) to regulate VCAM	immunological disorders,
				expression. For example,	neoplastic disorders (e.g.
				FMAT may be used to meaure	cancer/tumorigenesis), and
				the upregulation of cell surface	cardiovascular disorders (such
				VCAM-1 expresssion in	as described below under
				endothelial cells. Endothelial	"Immune Activity", "Blood-
				cells are cells that line blood	Related Disorders",
				vessels, and are involved in	"Hyperproliferative Disorders"
				functions that include, but are	and/or "Cardiovascular
				not limited to, angiogenesis,	Disorders"). Highly preferred
				vascular permeability, vascular	indications include neoplasms
				tone, and immune cell	and cancers such as, for
				extravasation. Exemplary	example, leukemia, lymphoma,
				endothelial cells that may be	melanoma, renal cell
				used according to these assays	carcinoma, and prostate,
				include human umbilical vein	breast, lung, colon, pancreatic,
				endothelial cells (HUVEC),	esophageal, stomach, brain,
				which are available from	liver and urinary cancer. Other
				commercial sources. The	preferred indications include
				expression of VCAM	benign dysproliferative
				(CD106), a membrane-	disorders and pre-neoplastic

conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.			A highly preferred indication is diabetes mellitus. Additional highly preferred indications include complications associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve	disease and nerve damage (e.g., due to diabetic
associated protein, can be upregulated by cytokines or other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses.			Assays for the regulation of transcription through the DMEF1 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the DMEF1 response element in a reporter construct (such as that containing the GLUT4	insulin production. The DMEF1 response element is
	SEAP in Jurkat/IL4 promoter (antiCD3 co-stim)	SEAP in Senescence Assay	Regulation of transcription via DMEF1 response element in adipocytes and preadipocytes	
	1136	1136	1137	
	HFCEW05	HFCEW05	HFFAD59	
,	188	188	189	

		nresent in the GLITT4	neuropathy), blood vessel	ood vessel
		promoter and binds to MEF2		blockage, heart disease, stroke,
		transcription factor and another	er	impotence (e.g., due to diabetic
	-	transcription factor that is		lood vessel
-		required for insulin regulation		ures, mental
		of Glut4 expression in skeletal		vsiness,
		muscle. GLUT4 is the primary		erglycemic-
		insulin-responsive glucose	e hyperosmolar coma,	oma,
		transporter in fat and muscle	cle   cardiovascular disease (e.g.,	disease (e.g.,
		tissue. Exemplary assays that	that heart disease, atherosclerosis,	therosclerosis,
		may be used or routinely	microvascular disease,	disease,
		modified to test for DMEF1		hypertension, stroke, and other
		response element activity (in	(in diseases and disorders as	sorders as
		adipocytes and pre-adipocytes)	ytes)   described in the	a)
		by polypeptides of the	"Cardiovascular Disorders"	ır Disorders"
		invention (including antibodies	odies   section below), dyslipidemia,	, dyslipidemia,
		and agonists or antagonists of	ts of endocrine disorders (as	rders (as
		the invention) include assays	ays described in the "Endocrine	e "Endocrine
		disclosed in Thai, M.V., et al., J		tion below),
		Biol Chem, 273(23):14285-92		neuropathy, vision impairment
		(1998); Mora, S., et al., J Biol		(e.g., diabetic retinopathy and
		Chem, 275(21):16323-8		blindness), ulcers and impaired
		(2000); Liu, M.L., et al., J Biol		, and infection
		Chem, 269(45):28514-21	(e.g., infectious diseases and	s diseases and
		(1994); "Identification of a 30-	a 30-	scribed in the
		base pair regulatory element	ent   "Infectious Diseases" section	seases" section
		and novel DNA binding	below, especially of the	lly of the
		protein that regulates the	urinary tract and skin). An	nd skin). An
		human GLUT4 promoter in	in additional highly preferred	lly preferred
		transgenic mice", J Biol Chem.		pesity and/or
		2000 Aug 4;275(31):23666-73;		complications associated with

	as T-cells).	the ability of polypeptides of	(e.g., as described below under
		the invention (including	"Immune Activity",
		antibodies and agonists or	"Cardiovascular Disorders",
		antagonists of the invention) to	and/or "Blood-Related
 		modulate growth and other cell	Disorders"), and infection
		functions. Exemplary assays	(e.g., an infectious disease as
		for transcription through the	described below under
		AP1 response element that	"Infectious Disease"). Highly
		may be used or routinely	preferred indications include
 		modified to test AP1-response	autoimmune diseases (e.g.,
		element activity of	rheumatoid arthritis, systemic
		polypeptides of the invention	lupus erythematosis, multiple
		(including antibodies and	sclerosis and/or as described
		agonists or antagonists of the	below) and
**.		invention) include assays	immunodeficiencies (e.g., as
		disclosed in Berger et al., Gene	described below). Additional
-		66:1-10 (1988); Cullen and	highly preferred indications
		Malm, Methods in Enzymol	include inflammation and
	-	216:362-368 (1992); Henthorn	inflammatory disorders.
		et al., Proc Natl Acad Sci USA	Highly preferred indications
-		85:6342-6346 (1988);	also include neoplastic
		Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
		272(49):30806-30811 (1997);	lymphoma, and/or as described
		Chang et al., Mol Cell Biol	below under
		18(9):4986-4993 (1998); and	"Hyperproliferative
*		Fraser et al., Eur J Immunol	Disorders"). Highly preferred
		29(3):838-844 (1999), the	indications include neoplasms
		contents of each of which are	and cancers, such as, leukemia,
		herein incorporated by	lymphoma, prostate, breast,
		reference in its entirety. T	lung, colon, pancreatic,
		cells that may be used	esophageal, stomach, brain,

				according to these assays are	liver, and urmary cancer. Ourer
				publicly available (e.g.,	preferred indications include
				through the ATCC).	benign dysproliferative
				Exemplary mouse T cells that	disorders and pre-neoplastic
				may be used according to these	conditions, such as, for
•				assays include the CTLL cell	example, hyperplasia,
				line, which is an IL-2	metaplasia, and/or dysplasia.
				dependent suspension-culture	Preferred indications include
•				cell line with cytotoxic	arthritis, asthma, AIDS,
			•	activity.	allergy, anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
		•••	•		transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HFFAD59	1137	Activation of	Assays for the activation of	A preferred embodiment of
			transcription	transcription through the	the invention includes a
	,	-	through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
	-			the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha

production. Preferred	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative
antagonists of the invention) to	regulate the serum response factors and modulate the	expression of genes involved	in growth. Exemplary assays	for transcription through the	SRE that may be used or	routinely modified to test SRE	activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell
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Disorders"). Additionally, highly preferred indications include neoplasms and	cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g.,	malignant glioma), solid tumors, and prostate, breast,	lung, colon, pancreatic, esophageal, stomach, brain,	liver and urinary cancer. Other	preterred indications include benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,
line, which is an IL-2 dependent suspension culture of T cells with cytotoxic	activity.																				-		
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	,				hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below
189	HFFAD59	1137	SEAP in Senescence Assay		under miceulous Disease ).
001	HFFAL36	1138	Activation of	Assays for the activation of	Preferred indications
061			through AP1	ranscription unough the Arri response element are known in	(e.g., as described below under
			response element in	the art and may be used or	"Hyperproliferative
			immune cells (such	routinely modified to assess	Disorders"), blood disorders
			as T-cells).	the ability of polypeptides of	(e.g., as described below under
				the invention (including	"Immune Activity",
				antibodies and agonists or	"Cardiovascular Disorders",
_				antagonists of the invention) to	and/or "Blood-Related
		*		modulate growth and other cell	Disorders"), and infection
_				functions. Exemplary assays	(e.g., an infectious disease as
				for transcription through the	described below under
				AP1 response element that	"Infectious Disease"). Highly
				may be used or routinely	preferred indications include
				modified to test AP1-response	autoimmune diseases (e.g.,
				element activity of	rheumatoid arthritis, systemic
				polypeptides of the invention	lupus erythematosis, multiple
				(including antibodies and	sclerosis and/or as described
				agonists or antagonists of the	below) and
				invention) include assays	immunodeficiencies (e.g., as

			disclosed in Berger et al., Gene	described below). Additional
			66:1-10 (1988); Cullen and	highly preferred indications
 ·		-	Malm, Methods in Enzymol	include inflammation and
			216:362-368 (1992); Henthorn	inflammatory disorders.
			et al., Proc Natl Acad Sci USA	Highly preferred indications
 			85:6342-6346 (1988);	also include neoplastic
			Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
			272(49):30806-30811 (1997);	lymphoma, and/or as described
			Chang et al., Mol Cell Biol	below under
			18(9):4986-4993 (1998); and	"Hyperproliferative
 			Fraser et al., Eur J Immunol	Disorders"). Highly preferred
	<u></u>		29(3):838-844 (1999), the	indications include neoplasms
		-	contents of each of which are	and cancers, such as, leukemia,
· ·			herein incorporated by	lymphoma, prostate, breast,
			reference in its entirety. T	lung, colon, pancreatic,
			cells that may be used	esophageal, stomach, brain,
 			according to these assays are	liver, and urinary cancer. Other
			publicly available (e.g.,	preferred indications include
-			through the ATCC).	benign dysproliferative
			Exemplary mouse T cells that	disorders and pre-neoplastic
			may be used according to these	conditions, such as, for
 			assays include the CTLL cell	example, hyperplasia,
 	,		line, which is an IL-2	metaplasia, and/or dysplasia.
			dependent suspension-culture	Preferred indications include
 			cell line with cytotoxic	arthritis, asthma, AIDS,
			activity.	allergy, anemia, pancytopenia,
				leukopenia, thrombocytopenia,
-				Hodgkin's disease, acute
<b>-</b> 9.				lymphocytic anemia (ALL),
				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,

					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
 	HFFAL36	1138	Activation of	Assays for the activation of	A preferred embodiment of
190			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
****				regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),
				routinely modified to test SRE	Highly preferred indications
				activity of the polypeptides of	include autoimmune diseases
				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,
				antagonists of the invention)	Crohn"s disease, multiple
				include assays disclosed in	sclerosis and/or as described
				Berger et al., Gene 66:1-10	below), immunodeficiencies
				(1998); Cullen and Malm,	(e.g., as described below),

boosting a T cell-mediated immune response, and suppressing a T cell-mediated	immune response. Additional highly preferred indications	include inflammation and	inflammatory disorders, and treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications			e and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for
Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); and Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the AICC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.											
																				•••			<b></b>			
																<u> </u>					_					

example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").		
	!	
·	IL-10 in Human T-cell 2B9	SEAP in HepG2/Squale- synthetase(stimulati on)
	1138	1139
	HFFAL36	HFGAD82
	190	191

	HFGAD82	1139	SEAP in HIB/CRE		
191					
	HFGAD82	1139	Activation of	Assays for the activation of	Preferred indications
191			transcription	transcription through the AP1	include neoplastic diseases
			through AP1	response element are known in	(e.g., as described below under
		·	response element in	the art and may be used or	"Hyperproliferative
			immune cells (such	routinely modified to assess	Disorders"), blood disorders
			as T-cells).	the ability of polypeptides of	(e.g., as described below under
				the invention (including	"Immune Activity",
				antibodies and agonists or	"Cardiovascular Disorders",
				antagonists of the invention) to	and/or "Blood-Related
				modulate growth and other cell	Disorders"), and infection
				functions. Exemplary assays	(e.g., an infectious disease as
		***		for transcription through the	described below under
				AP1 response element that	"Infectious Disease"). Highly
				may be used or routinely	preferred indications include
				modified to test AP1-response	autoimmune diseases (e.g.,
				element activity of	rheumatoid arthritis, systemic
				polypeptides of the invention	lupus erythematosis, multiple
				(including antibodies and	sclerosis and/or as described
				agonists or antagonists of the	below) and
				invention) include assays	immunodeficiencies (e.g., as
				disclosed in Berger et al., Gene	described below). Additional
				66:1-10 (1988); Cullen and	highly preferred indications
				Malm, Methods in Enzymol	include inflammation and
				216:362-368 (1992); Henthorn	inflammatory disorders.
				et al., Proc Natl Acad Sci USA	Highly preferred indications
		-		85:6342-6346 (1988);	also include neoplastic
				Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
				272(49):30806-30811 (1997);	lymphoma, and/or as described
				Chang et al., Mol Cell Biol	below under

				18/0):4086-4003 (1008): and	"Hynernroliferative
		1.7			Disorders"). Highly preferred
				29(3):838-844 (1999), the	indications include neoplasms
				contents of each of which are	and cancers, such as, leukemia,
				herein incorporated by	lymphoma, prostate, breast,
				reference in its entirety.	lung, colon, pancreatic,
				Mouse T cells that may be	esophageal, stomach, brain,
				used according to these assays	liver, and urinary cancer. Other
				are publicly available (e.g.,	preferred indications include
				through the ATCC).	benign dysproliferative
				Exemplary mouse T cells that	disorders and pre-neoplastic
				may be used according to these	conditions, such as, for
				assays include the HTZ cell	example, hyperplasia,
				line, which is an IL-2	metaplasia, and/or dysplasia.
				dependent suspension culture	Preferred indications include
				cell line that also responds to	arthritis, asthma, AIDS,
		g		IL-4.	allergy, anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
		·			myeloma, Burkitt's lymphoma,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HFGAD82	1139	Stimulation of	Assays for measuring secretion	A highly preferred
191			insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
					) ·

from pancreatic	the art and may be used or	An additional highly preferred
heta cells.	routinely modified to assess	indication is a complication
0000	the obility of notineating of	minimum is a comprison on a
41-	the ability of polypeptides of	associated will diadetes (e.g.,
	the invention (including	diabetic retinopathy, diabetic
	antibodies and agonists or	nephropathy, kidney disease
	antagonists of the invention) to	(e.g., renal failure,
	stimulate insulin secretion.	nephropathy and/or other
	For example, insulin secretion	diseases and disorders as
	is measured by FMAT using	described in the "Renal
	anti-rat insulin antibodies.	Disorders" section below),
	Insulin secretion from	diabetic neuropathy, nerve
	pancreatic beta cells is	disease and nerve damage
	upregulated by glucose and	(e.g., due to diabetic
	also by certain	neuropathy), blood vessel
	proteins/peptides, and	blockage, heart disease, stroke,
	disregulation is a key	impotence (e.g., due to diabetic
	component in diabetes.	neuropathy or blood vessel
	Exemplary assays that may be	blockage), seizures, mental
	used or routinely modified to	confusion, drowsiness,
	test for stimulation of insulin	nonketotic hyperglycemic-
	secretion (from pancreatic	hyperosmolar coma,
	cells) by polypeptides of the	cardiovascular disease (e.g.,
	invention (including antibodies	heart disease, atherosclerosis,
	and agonists or antagonists of	microvascular disease,
	the invention) include assays	hypertension, stroke, and other
	disclosed in: Ahren, B., et al.,	diseases and disorders as
	Am J Physiol, 277(4 Pt	described in the
	2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
	al., Endocrinology,	section below), dyslipidemia,
	138(9):3735-40 (1997); Kim,	endocrine disorders (as
	K.H., et al., FEBS Lett,	described in the "Endocrine

				377(2):237-9 (1995); and,	Disorders" section below),
			,-	Miraglia S et. al., Journal of	neuropathy, vision impairment
	١			Biomolecular Screening,	(e.g., diabetic retinopathy and
	-			4:193-204 (1999), the contents	blindness), ulcers and impaired
				of each of which is herein	wound healing, and infection
	•			incorporated by reference in its	(e.g., infectious diseases and
				entirety. Pancreatic cells that	disorders as described in the
				may be used according to these	"Infectious Diseases" section
				assays are publicly available	below, especially of the
				(e.g., through the ATCC)	urinary tract and skin), carpal
				and/or may be routinely	tunnel syndrome and
••				generated. Exemplary	Dupuytren's contracture).
		,-		pancreatic cells that may be	An additional highly preferred
				used according to these assays	indication is obesity and/or
				include rat INS-1 cells. INS-1	complications associated with
				cells are a semi-adherent cell	obesity. Additional highly
				line established from cells	preferred indications include
		•		isolated from an X-ray induced	weight loss or alternatively,
				rat transplantable insulinoma.	weight gain. Aditional
			1	These cells retain	highly preferred indications are
				characteristics typical of native	complications associated with
				pancreatic beta cells including	insulin resistance.
				glucose inducible insulin	
				secretion. References: Asfari	
				et al. Endocrinology 1992	
				130:167.	
	HFIIZ70	1140	Activation of JNK	Kinase assay. JNK kinase	Highly preferred indications
			Signaling Pathway	assays for signal transduction	include asthma, allergy,
			in immune cells	that regulate cell proliferation,	hypersensitivity reactions,
			(such as	activation, or apoptosis are	inflammation, and
			eosinophils).	well known in the art and may	inflammatory disorders.

Additional highly preferred indications include immune and hematopoietic disorders	(e.g., as described below under "Immune Activity", and	"Blood-Related Disorders"), autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, Cronn's disease, multiple sclerosis	and/or as described below),	immunodeficiencies (e.g., as	preferred indications also	include boosting or inhibiting	immune cell proliferation.	Preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as	described below under	"Hyperproliferative	Disorders"). Highly preferred	indications include boosting an	eosinophil-mediated immune	response, and suppressing an	eosinophil-mediated immune	response.				
be used or routinely modified to assess the ability of molynentides of the invention	(including antibodies and agonists or antagonists of the	invention) to promote or inhibit cell proliferation,	activation, and apoptosis.	Exemplary assays for JNK kinase activity that may be	used or routinely modified to	test JNK kinase-induced	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Gupta et al., Exp	Cell Res 247(2): 495-504	(1999); Kyriakis JM, Biochem	Soc Symp 64:29-48 (1999);	Chang and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Exemplary cells that may be	used according to these assays
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include eosinophils.	Eosinophils are important in	the late stage of allergic	reactions; they are recruited to	tissues and mediate the	inflammatory response of late	stage allergic reaction.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and	activation of c-Jun NH2-	terminal kinase and p38	mitogen-activated protein	kinase in human eosinophils"	Clin Exp Immunol;	Oct;122(1):20-7 (2000);	Hebestreit H, et al.,	"Disruption of fas receptor	signaling by nitric oxide in	eosinophils" J Exp Med; Feb
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	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of asthma, allergy, hypersensitivity and inflammation.
2;187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate caspase protease-mediated apoptosis in immune cells (such as, for example, in mast cells). Mast cells are found in connective and mucosal tissues throughout
	Regulation of apoptosis of immune cells (such as mast cells).
	1141
	HFKET18
	193

the body, and their activation	via immunoglobulin E -	antigen, promoted by T helper	cell type 2 cytokines, is an	important component of	allergic disease. Dysregulation	of mast cell apoptosis may	play a role in allergic disease	and mast cell tumor survival.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	capase apoptosis activity	induced by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in: Masuda A,	et al., J Biol Chem,	276(28):26107-26113 (2001);	Yeatman CF 2nd, et al., J Exp	Med, 192(8):1093-1103	(2000); Lee et al., FEBS Lett	485(2-3): 122-126 (2000); Nor	et al., J Vasc Res 37(3): 209-	218 (2000); and Karsan and	Harlan, J Atheroscler Thromb	3(2): 75-80 (1996); the	contents of each of which are	herein incorporated by	reference in its entirety.
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				Immine cells that may be used	
				according to these assays are	
				publicly available (e.g.,	
				through commercial sources).	
				Exemplary immune cells that	
	-			may be used according to these	
				assays include mast cells such	
				as the HMC human mast cell	
				line.	
	HFKET18	1141	Activation of	Assays for the activation of	Highly preferred indications
193			transcription	transcription through the	include blood disorders (e.g.,
			through NFAT	Nuclear Factor of Activated T	as described below under
			response in immune	cells (NFAT) response element	"Immune Activity", "Blood-
			cells (such as T-	are well-known in the art and	Related Disorders", and/or
			cells).	may be used or routinely	"Cardiovascular Disorders").
				modified to assess the ability	Highly preferred indications
				of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
			-	and agonists or antagonists of	systemic lupus erythematosis,
				the invention) to regulate	multiple sclerosis and/or as
				NFAT transcription factors and	described below),
				modulate expression of genes	immunodeficiencies (e.g., as
				involved in	described below), boosting a T
				immunomodulatory functions.	cell-mediated immune
_				Exemplary assays for	response, and suppressing a T
				transcription through the	cell-mediated immune
				NFAT response element that	response. Additional highly
				may be used or routinely	preferred indications include
				modified to test NFAT-	inflammation and
				response element activity of	inflammatory disorders. An
				polypeptides of the invention	additional highly preferred

		;	(including antibodies and	indication is infection (e.g., an
			agonists or antagonists of the	infectious disease as described
			invention) include assays	below under "Infectious
			disclosed in Berger et al., Gene	Disease"). Preferred
	_		66:1-10 (1998); Cullen and	indications include neoplastic
			Malm, Methods in Enzymol	diseases (e.g., leukemia,
			216:362-368 (1992); Henthorn	lymphoma, and/or as described
			et al., Proc Natl Acad Sci USA	below under
			85:6342-6346 (1988); Serfling	"Hyperproliferative
			et al., Biochim Biophys Acta	Disorders"). Preferred
			1498(1):1-18 (2000); De Boer	indications include neoplasms
	-		et al., Int J Biochem Cell Biol	and cancers, such as, for
			31(10):1221-1236 (1999);	example, leukemia, lymphoma,
`			Fraser et al., Eur J Immunol	and prostate, breast, lung,
	,		29(3):838-844 (1999); and	colon, pancreatic, esophageal,
-			Yeseen et al., J Biol Chem	stomach, brain, liver and
			268(19):14285-14293 (1993),	urinary cancer. Other preferred
			the contents of each of which	indications include benign
	_		are herein incorporated by	dysproliferative disorders and
			reference in its entirety. T	pre-neoplastic conditions, such
			cells that may be used	as, for example, hyperplasia,
			according to these assays are	metaplasia, and/or dysplasia.
			publicly available (e.g.,	Preferred indications also
			through the ATCC).	include anemia, pancytopenia,
			Exemplary human T cells that	leukopenia, thrombocytopenia,
			may be used according to these	Hodgkin's disease, acute
	,		assays include the JURKAT	lymphocytic anemia (ALL),
			cell line, which is a suspension	plasmacytomas, multiple
			culture of leukemia cells that	myeloma, Burkitt's lymphoma,
			produce IL-2 when stimulated.	arthritis, AIDS, granulomatous
				disease, inflammatory bowel

disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	inase assays,  A highly preferred embodiment of the invention includes a method for regulate cell lifferentiation n the art and outinely in the art and outinely in the art and outinely in the art and outinely ling antibodies  promote or intagonists of the invention includes a method for inhibiting natural killer cell proliferation. An lifferentiation. Includes a method for inhibiting natural killer cell differentiation. Highly preferred indications include ling antibodies highly preferred indications include described below under
	Activation of Kinase assay. Kinase assays, Natural Killer Cell for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of
	Activation of Natural Killer C ERK Signaling Pathway.
	HFKET18

Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders",	and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under "Immune Activity") and	infections (e.g., as described below under "Infectious Disease"). Preferred include blood	disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or	"Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as	described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders.  Highly preferred indications	also include cancers such as, kidney, melanoma, prostate,
assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Kyriakis JM, Biochem Soc Symp 64:29-48	(1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-	500 (1999); the contents of each of which are herein incorporated by reference in its	that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary natural	killer cells that may be used according to these assays include the human natural killer cell lines (for example, NK-YT cells which have	activity) or primary NK cells.	

					breast, lung, colon, pancreatic,
					esophageal, stomach, brain,
					liver, urinary cancer,
					lymphoma and leukemias.
					Other preferred indications
					include benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
					Other highly preferred
					indications include,
					pancytopenia, leukopenia,
					leukemias, Hodgkin's disease,
					acute lymphocytic anemia
					(ALL), arthritis, asthma,
					AIDS, granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, immune
					reactions to transplanted
					organs and tissues,
	-				endocarditis, meningitis, Lyme
					Disease, and allergies.
	HFKFG02	1142	Activation of	Kinase assay. Kinase assays,	A highly preferred
194			Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
			Signaling Pathway	assay, for ERK signal	includes a method for
				transduction that regulate cell	stimulating adipocyte
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment
				may be used or routinely	of the invention includes a
				modified to assess the ability	method for inhibiting

le adipocyte proliferation. A	ntibodies	gonists of   of the invention includes a		tion, adipocyte differentiation. An		or ERK   embodiment of the invention	nay be   includes a method for	odified to inhibiting adipocyte		des of the preferred embodiment of the	antibodies   invention includes a method	gonists of   for stimulating (e.g.,	de the increasing) adipocyte	Forrer et   activation. An alternative	8-9):1101-   highly preferred embodiment	rchand- of the invention includes a	method for inhibiting the					(e.g., as described below under		ophys Mol   Highly preferred indications	00 (1999);   also include neoplastic			rety. described below under		1
of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to promote or	inhibit cell proliferation,	activation, and differentiation.	Exemplary assays for ERK	kinase activity that may be	used or routinely modified to	test ERK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Le Marchand-	Brustel Y, Exp Clin	Endocrinol Diabetes	107(2):126-132 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Mouse adipocyte cells that	
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indications include blood disorders (e.g., hypertension, congestive heart failure, blood vessel blockage, heart disease, stroke, impotence and/or as	described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under	"Immune Activity"), neural disorders (e.g., as described below under "Neural Activity and Neurological Diseases"), and infection (e.g., as described below under	A highly preferred indication is diabetes mellitus. An additional highly preferred indication associated with diabetes (e.g., diabetic retinopathy, diabetic	nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve
assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays	include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and	undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.		

disease and nerve damage	(e.g., due to diabetic neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred
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indication is obesity and/or complications associated with obesity. Additional highly preferred indications include	weight loss or alternatively, weight gain. Additional highly preferred indications are	insulin resistance. Additional highly preferred indications are disorders of the	musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein.	Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia,	gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred	indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney	indications include melanoma, prostate, lung, pancreatic,
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esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.		Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and
		Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the
	IL-10 in Human T-cell 293T	Activation of transcription through AP1 response element in immune cells (such as T-cells).
	1142	1143
	HFKFG02	HFOXB13
	194	195

immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and	inflammatory disorders. Highly preferred indications also include neoplastic	diseases (e.g., leukemia, lymphoma, and/or as described below under "Hynernroliferative"	Disorders"). Highly preferred indications include neoplasms	and cancers, such as, leukemia,	lung, colon, pancreatic,	esophageal, stomach, brain, liver, and urinary cancer. Other	preferred indications include benign dysproliferative	disorders and pre-neoplastic conditions, such as, for		Preferred indications include	arthritis, asthma, AIDS,	allergy, anemia, pancytopenia, leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),
invention) include assays disclosed in Berger et al., Gene 66:1-10 (1988); Cullen and Malm, Methods in Enzymol	216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988);	Kellahan et al., J Biol Chem 272(49):30806-30811 (1997); Chang et al., Mol Cell Biol 18(9):4986-4993 (1998): and	Fraser et al., Eur J Immunol 29(3):838-844 (1999), the	contents of each of which are	reference in its entirety.	Mouse T cells that may be used according to these assays	are publicly available (e.g., through the ATCC).	Exemplary mouse T cells that may be used according to these	assays include the HTZ cell	dependent suspension culture	cell line that also responds to	IL-4.		
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myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of asthma, allergy, hypersensitivity and inflammation.
	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate caspase protease-mediated apoptosis in immune cells (such as, for example, in mast cells). Mast cells are found in connective and mucosal tissues throughout the body, and their activation via immunoglobulin E - antigen, promoted by T helper cell type 2 cytokines, is an important component of allergic disease. Dysregulation of mast cell apoptosis may play a role in allergic disease and mast cell tumor survival.
	Regulation of apoptosis of immune cells (such as mast cells).
	1144
	HFPAC12
	196

Exemplary assays for caspase anontosis that may be used or	routinely modified to test	capase apoptosis activity	induced by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in: Masuda A,	et al., J Biol Chem,	276(28):26107-26113 (2001);	Yeatman CF 2nd, et al., J Exp	Med, 192(8):1093-1103	(2000);Lee et al., FEBS Lett	485(2-3): 122-126 (2000); Nor	et al., J Vasc Res 37(3): 209-	218 (2000); and Karsan and	Harlan, J Atheroscler Thromb	3(2): 75-80 (1996); the	contents of each of which are	herein incorporated by	reference in its entirety.	Immune cells that may be used	according to these assays are	publicly available (e.g.,	through commercial sources).	Exemplary immune cells that	may be used according to these	assays include mast cells such	as the HMC human mast cell	line,
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196	HFPAC12	1144	IFNg in Human T-cell 2B9		
196	HFPAC12	1144	IL-2 in Human T-cell 2B9		
	HFPA071	1145	Activation of JNK	Kinase assay. JNK kinase	Highly preferred indications
197			Signaling Pathway	assays for signal transduction	include asthma, allergy,
			in immune cells	that regulate cell proliferation,	hypersensitivity reactions,
			(such as	activation, or apoptosis are	inflammation, and
			eosinophils).	well known in the art and may	inflammatory disorders.
				be used or routinely modified	Additional highly preferred
				to assess the ability of	indications include immune
				polypeptides of the invention	and hematopoietic disorders
				(including antibodies and	(e.g., as described below under
				agonists or antagonists of the	"Immune Activity", and
				invention) to promote or	"Blood-Related Disorders"),
				inhibit cell proliferation,	autoimmune diseases (e.g.,
				activation, and apoptosis.	rheumatoid arthritis, systemic
				Exemplary assays for JNK	lupus erythematosis, Crohn"s
				kinase activity that may be	disease, multiple sclerosis
				used or routinely modified to	and/or as described below),
				test JNK kinase-induced	immunodeficiencies (e.g., as
				activity of polypeptides of the	described below). Highly
				invention (including antibodies	preferred indications also
				and agonists or antagonists of	include boosting or inhibiting
				the invention) include the	immune cell proliferation.
				assays disclosed in Forrer et	Preferred indications include
				al., Biol Chem 379(8-9):1101-	neoplastic diseases (e.g.,
				1110 (1998); Gupta et al., Exp	leukemia, lymphoma, and/or as
		•••		Cell Res 247(2): 495-504	described below under
				(1999); Kyriakis JM, Biochem	"Hyperproliferative
				Soc Symp 64:29-48 (1999);	Disorders"). Highly preferred

indications include boosting an	response, and suppressing an	eosinophil-mediated immune	response.																										
Chang and Karin, Nature	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Exemplary cells that may be	used according to these assays	include eosinophils.	Eosinophils are important in	the late stage of allergic	reactions; they are recruited to	tissues and mediate the	inflammatory response of late	stage allergic reaction.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and	activation of c-Jun NH2-
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	Highly preferred indications include eosinophilia, asthma, allergy, hypersensitivity reactions, inflammation, and inflammatory disorders
terminal kinase and p38 mitogen-activated protein kinase in human eosinophils" Clin Exp Immunol; Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils" J Exp Med; Feb 2;187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N- terminal kinase and failure of prednisolone to inhibit JUN N- terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	Assay that measures the production of the chemokine interleukin-8 (IL-8) from immune cells (such as the EOL-1 human eosinonhil cell
	Production of IL-8 by immune cells (such as the human EOL-1 eosinophil cells)
	1145
TO YOUR	HFPAO71
	197

			IL-8 production by FMA1) and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit. Eosinophils are a type of immune cell important in allergic responses; they are recruited to tissues and mediate the inflammtory response of late stage allergic reaction. IL8 is a strong immunomodulator and may have a potential proinflammatory role in immunological diseases and disorders (such as allergy and asthma).	and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting or inhibiting immune cell proliferation. Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include boosting an eosinophil-mediated immune response, and suppressing an activated indications include boosting an eosinophil-mediated immune response, and suppressing an
HFPA071	1145	Production of IL-8 by by endothelial cells (such as Human Umbilical	Assays measuring production of IL-8 are well known in the art and may be used or routinely modified to assess	response. Highly preferred indications include immunological and inflammatory disorders (e.g., such as allergy, asthma,

				such as neutrophils, macrophages, and lymphocytes.	
	HFPCX09	1146	Production of TNF	TNFa FMAT. Assays for	A highly preferred
198			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for
				macrophages, T cells,	inhibiting (e.g., decreasing)
				fibroblasts, smooth muscle,	TNF alpha production. An
, ,=				and other cell types that exert a	alternative highly preferred
				wide variety of inflammatory	embodiment of the invention
				and cytotoxic effects on a	includes a method for
				variety of cells are well known	stimulating (e.g., increasing)
				in the art and may be used or	TNF alpha production.
				routinely modified to assess	Highly preferred indications
				the ability of polypeptides of	include blood disorders (e.g.,
				the invention (including	as described below under
				antibodies and agonists or	"Immune Activity", "Blood-
				antagonists of the invention) to	Related Disorders", and/or
				mediate immunomodulation,	"Cardiovascular Disorders"),
				modulate inflammation and	Highly preferred indications
				cytotoxicity. Exemplary	include autoimmune diseases
				assays that test for	(e.g., rheumatoid arthritis,
				immunomodulatory proteins	systemic lupus erythematosis,
				evaluate the production of	Crohn"s disease, multiple
				cytokines such as tumor	sclerosis and/or as described
				necrosis factor alpha (TNFa),	below), immunodeficiencies
				and the induction or inhibition	(e.g., as described below),
				of an inflammatory or	boosting a T cell-mediated
				cytotoxic response. Such	immune response, and
				assays that may be used or	suppressing a T cell-mediated
				routinely modified to test	immune response. Additional

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highly preferred indications include inflammation and inflammatory disorders, and	treating joint damage in patients with rheumatoid			Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliterative	Disorders'). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, leukemia,	lymphoma, melanoma, glioma	(e.g., malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukonenia thromhocytonenia
immunomodulatory activity of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Verhasselt et al., Eur J	Immunol 28(11):3886-3890	(1198); Dahlen et al., J	Immunol 160(7):3585-3593	(1998); Verhasselt et al., J	Immunol 158:2919-2925	(1997); and Nardelli et al., J	Leukoc Biol 65:822-828	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which,	when activated by antigen	and/or extolines initiate and
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			*	upregulate T cell proliferation and functional activities.	Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious
PC	HFPCX09	1146	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the	disease as described below under "Infectious Disease"). Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders.  Preferred indications also include blood disorders (e.g.,

as described below under "Immune Activity", "Blood- Related Disorders", and/or	"Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g.,	rheumatoid arthritis, systemic lupus erythematosis, multiple	sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,
art and may be used or routinely modified to assess the ability of polypeptides of	the invention (including antibodies and agonists or antagonists of the invention) to	regulate GATA3 transcription factors and modulate	expression of mast cell genes important for immune response	development. Exemplary assays for transcription	through the GATA3 response	element that may be used or routinely modified to test	GATA3-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell	et al., Cold Spring Harb Symp	Quant Biol 64:563-571 (1999);	Rodriguez-Palmero et al., Eur	J Immunol 29(12):3914-3924	(1999); Zheng and Flavell,
									<del></del>				12									

				Cell 89(4):587-596 (1997); and Henderson et al., Mol Cell Biol	acute lymphocytic anemia (ALL), plasmacytomas,
				14(6):4286-4294 (1994), the contents of each of which are	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
				herein incorporated by	granulomatous disease,
				reference in its entirety. Mast	inflammatory bowel disease,
				cells that may be used	sepsis, neutropenia,
				according to these assays are	neutrophilia, psoriasis,
				publicly available (e.g.,	suppression of immune
		,		through the ATCC).	reactions to transplanted
				Exemplary human mast cells	organs and tissues, hemophilia,
				that may be used according to	hypercoagulation, diabetes
				these assays include the HMC-	mellitus, endocarditis,
				1 cell line, which is an	meningitis, and Lyme Disease.
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HFPCX09	1146	Activation of	This reporter assay measures	Highly preferred indications
198			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,

	response element are well-	as described below under
 	known in the art and may be	"Immune Activity", "Blood-
	used or routinely modified to	Related Disorders", and/or
	assess the ability of	"Cardiovascular Disorders").
	polypeptides of the invention	Preferred indications include
	(including antibodies and	autoimmune diseases (e.g.,
	agonists or antagonists of the	rheumatoid arthritis, systemic
	invention) to regulate NFAT	lupus erythematosis, multiple
 	transcription factors and	sclerosis and/or as described
	modulate expression of genes	below) and
	involved in	immunodeficiencies (e.g., as
	immunomodulatory functions.	described below). Preferred
	Exemplary assays for	indications include neoplastic
	transcription through the	diseases (e.g., leukemia,
	NFAT response element that	lymphoma, melanoma,
	may be used or routinely	prostate, breast, lung, colon,
 	modified to test NFAT-	pancreatic, esophageal,
 	response element activity of	stomach, brain, liver, and
	polypeptides of the invention	urinary tract cancers and/or as
,	(including antibodies and	described below under
	agonists or antagonists of the	"Hyperproliferative
	invention) include assays	Disorders"). Other preferred
	disclosed in Berger et al., Gene	indications include benign
	66:1-10 (1998); Cullen and	dysproliferative disorders and
	Malm, Methods in Enzymol	pre-neoplastic conditions, such
	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
	85:6342-6346 (1988); De Boer	Preferred indications include
	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
	31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
	et al., J Immunol	leukemias, Hodgkin's disease,

				165(12):7215-7223 (2000):	acute lymphocytic anemia
				Hutchinson and McCloskey, I	(VII) plasmachmos
				Biol Chem 270(27):16333-	multiple myeloma Burkitt's
				16338 (1995), and Turner et	lymphoma, arthritis, AIDS.
				al., J Exp Med 188:527-537	granulomatous disease,
				(1998), the contents of each of	inflammatory bowel disease,
				which are herein incorporated	sepsis, neutropenia,
				by reference in its entirety.	neutrophilia, psoriasis,
				Mast cells that may be used	suppression of immune
				according to these assays are	reactions to transplanted
				publicly available (e.g.,	organs and tissues, hemophilia,
				through the ATCC).	hypercoagulation, diabetes
				Exemplary human mast cells	mellitus, endocarditis,
				that may be used according to	meningitis, and Lyme Disease.
····				these assays include the HMC-	
			•	1 cell line, which is an	
				immature human mast cell line	
	P-4-72-12-04			established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
198	HFPCX09	1146	VEGF in HT1080		
	HFPCX09	1146	IL-12 in Human B	and the state of t	
198			cells		
	HFPCX09	1146	IFNg in Human T-		
198			cell 293T		
	HFPCX09	1146	IL-2 in Human T-		
198			cell 293T		
	HFPCX36	1147	SEAP in		
				The state of the s	

199			Senescence Assay		
	HFPCX36	1147	Activation of	Assays for the activation of	Highly preferred indications
199			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as T-cells).	to assess the ability of	as described below under
				polypeptides of the invention	"Immune Activity", "Blood-
				(including antibodies and	Related Disorders", and/or
				agonists or antagonists of the	"Cardiovascular Disorders").
				invention) to regulate NFKB	Highly preferred indications
				transcription factors and	include autoimmune diseases
				modulate expression of	(e.g., rheumatoid arthritis,
				immunomodulatory genes.	systemic lupus erythematosis,
			4	Exemplary assays for	multiple sclerosis and/or as
-				transcription through the	described below), and
	_			NFKB response element that	immunodeficiencies (e.g., as
				may be used or rountinely	described below). An
				modified to test NFKB-	additional highly preferred
				response element activity of	indication is infection (e.g.,
				polypeptides of the invention	AIDS, and/or an infectious
				(including antibodies and	disease as described below
				agonists or antagonists of the	under "Infectious Disease").
				invention) include assays	Highly preferred indications
				disclosed in Berger et al., Gene	include neoplastic diseases
				66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
•				Malm, Methods in Enzymol	lymphoma, and/or as described
				216:362-368 (1992); Henthorn	below under
				et al., Proc Natl Acad Sci USA	"Hyperproliferative
				85:6342-6346 (1988); Black et	Disorders"). Highly preferred
				al., Virus Gnes 15(2):105-117	indications include neoplasms

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and cancers, such	as,melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	suppression of immune	reactions to transplanted	organs, asthma and allergy.
(1997); and Fraser et al.,	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the SUPT cell	line, which is a suspension	culture of IL-2 and IL-4	responsive T cells.																
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	HFRAN90	1148	Activation of	Assays for the activation of	Highly preferred indications
200			transcription	transcription through the	include neoplastic diseases
			through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
			response element in	Site (GAS) response element	and/or as described below
			immune cells (such	are well-known in the art and	under "Hyperproliferative
			as T-cells).	may be used or routinely	Disorders"). Highly preferred
				modified to assess the ability	indications include neoplasms
				of polypeptides of the	and cancers, such as, for
				invention (including antibodies	example, leukemia, lymphoma
				and agonists or antagonists of	(e.g., T cell lymphoma,
				the invention) to regulate	Burkitt's lymphoma, non-
				STAT transcription factors and	Hodgkins lymphoma,
				modulate gene expression	Hodgkin"s disease),
				involved in a wide variety of	melanoma, and prostate,
				cell functions. Exemplary	breast, lung, colon, pancreatic,
		***		assays for transcription	esophageal, stomach, brain,
				through the GAS response	liver and urinary cancer. Other
				element that may be used or	preferred indications include
				routinely modified to test	benign dysproliferative
				GAS-response element activity	disorders and pre-neoplastic
	ust Manual vol			of polypeptides of the	conditions, such as, for
				invention (including antibodies	example, hyperplasia,
				and agonists or antagonists of	metaplasia, and/or dysplasia.
				the invention) include assays	Preferred indications include
				disclosed in Berger et al., Gene	autoimmune diseases (e.g.,
				66:1-10 (1998); Cullen and	rheumatoid arthritis, systemic
				Malm, Methods in Enzymol	lupus erythematosis, multiple
				216:362-368 (1992); Henthorn	sclerosis and/or as described
				et al., Proc Natl Acad Sci USA	below), immunodeficiencies
				85:6342-6346 (1988);	(e.g., as described below),
				Matikainen et al., Blood	boosting a T cell-mediated

immune response, and suppressing a T cell-mediated immune response. Additional preferred indications include inflammation and inflammatory disorders.	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or	"Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant	osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include	anemia, pancytopenia, leukopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease,
93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety.	Exemplary human T cells, such as the MOLT4 cell line, that may be used according to these assays are publicly available (e.g., through the	ATCC).		

500	HFRAN90	1148	Production of ICAM-1	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein	sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.  Preferred embodiments of the invention include using polypeptides of the invention or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
				incorporated by reference in its entirety. Cells that may be	
				used according to these assays	

·	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Neurological Diseases and Disorders (e.g. Alzheimer"s Disease, Parkinson"s Disease, Brain Cancer, Seizures).	
are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of neuronal genes. Exemplary assays for transcription through the NFKB response element that may be used or routinely modified to test	activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Gill JS, et al., Neurobiol Dis, 7(4):448-461
	Activation of transcription through NFKB response element in neuronal cells (such as SKNMC cells).	
	1149	
	HFTCU19	
	201	

	HFTDL56	1150	Activation of	2000); Tamatani M, et al., J Biol Chem, 274(13):8531-8538 (1999); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Neuronal cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary neuronal cells that may be used according to these assays include the SKNMC neuronal cell line.	A preferred embodiment of
202			transcription through serum response element in	transcription through the Serum Response Element (SRE) are well-known in the	the invention includes a method for inhibiting (e.g., reducing) TNF alpha
,			immune cells (such as T-cells).	art and may be used or routinely modified to assess	production. An alternative preferred embodiment of the

invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred	indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or	"Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis,	systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described	below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and	immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and	treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases
the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to	regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the	SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including	antibodies and agonists or antagonists of the invention) include assays disclosed in	Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci 118 A	85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are	herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC).
	N					

(e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally,	highly preferred indications include neoplasms and cancers, such as, for example,	leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid	tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain,	liver and urinary cancer. Other preferred indications include	benign dysproliferative disorders and pre-neoplastic conditions, such as, for	example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include	anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute	lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous disease, inflammatory bowel	disease, neutropenia, neutrophilia, psoriasis.
Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2	dependent suspension culture of T cells with cytotoxic activity.									

suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").		Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
		Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-
	IL-6 in HUVEC	Production of ICAM-1
	1150	1150
	HFTDL56	HFTDL56
	202	202

		A Line 1.	A mgmy preferred	embodiment of the invention	includes a method for	stimulating endothelial cell	growth. An alternative highly	preferred embodiment of the	invention includes a method	for inhibiting endothelial cell	growth. A highly preferred	embodiment of the invention	includes a method for	stimulating endothelial cell	proliferation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting	endothelial cell proliferation.
each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).		Caspase Anontosis Dagge	caspase Apoptosis Nescue.	Assays for caspase apoptosis	rescue are well known in the	art and may be used or	routinely modified to assess	the ability of the polypeptides	of the invention (including	antibodies and agonists or	antagonists of the invention) to	inhibit caspase protease-	mediated apoptosis.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	caspase apoptosis rescue of	polypeptides of the invention	(including antibodies and
	SEAP in UMR-106	Protection from	F. J. J. J. J. 1.	Endothelial Cell	Apoptosis.														
·	1150	1151	( ) ( (		*														
	HFTDL56	HFTDZ36																	
	202		203	507															

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	4.	agomets of antagomets of the	A nigniy preferred
-	<u> </u>	invention) include the assays	embodiment of the invention
	- di	disclosed in Romeo et al.,	includes a method for
	<u></u>	Cardiovasc Res 45(3): 788-794	stimulating endothelial cell
	(2	(2000); Messmer et al., Br J	growth. An alternative highly
	<u>Z</u>	Pharmacol 127(7): 1633-1640	preferred embodiment of the
		(1999); and J Atheroscler	invention includes a method
-		Thromb 3(2): 75-80 (1996);	for inhibiting endothelial cell
	th	the contents of each of which	growth. A highly preferred
	ar	are herein incorporated by	embodiment of the invention
	re	reference in its entirety.	includes a method for
	<u> </u>	Endothelial cells that may be	stimulating apoptosis of
	sn	used according to these assays	endothelial cells. An
	ar	are publicly available (e.g.,	alternative highly preferred
	th	through commercial sources).	embodiment of the invention
	<u> </u>	Exemplary endothelial cells	includes a method for
	th	that may be used according to	inhibiting (e.g., decreasing)
	th	these assays include bovine	apoptosis of endothelial cells.
	ao	aortic endothelial cells	A highly preferred
	<u>(b)</u>	(bAEC), which are an example	embodiment of the invention
	Jo	of endothelial cells which line	includes a method for
	919	blood vessels and are involved	stimulating angiogenisis. An
		in functions that include, but	alternative highly preferred
	are	are not limited to,	embodiment of the invention
	an	angiogenesis, vascular	includes a method for
	be	permeability, vascular tone,	inhibiting angiogenesis. A
	an	and immune cell extravasation.	highly preferred embodiment
			of the invention includes a
			method for reducing cardiac
			hypertrophy. An alternative
			highly preferred embodiment

of the invention includes a method for inducing cardiac hypertrophy. Highly preferred indications include neonlastic diseases (e.g., as	described below under "Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive	heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular	disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under	"Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the

•			arteries, capillaries, veins
			and/or lymphatics). Highly
			preferred are indications that
			stimulate angiogenesis and/or
			cardiovascularization. Highly
			preferred are indications that
:			inhibit angiogenesis and/or
		 	cardiovascularization.
			Highly preferred indications
			include antiangiogenic activity
			to treat solid tumors,
			leukemias, and Kaposi"s
			sarcoma, and retinal disorders.
			Highly preferred indications
			include neoplasms and cancer,
			such as, Kaposi"s sarcoma,
			hemangioma (capillary and
			cavernous), glomus tumors,
			telangiectasia, bacillary
			angiomatosis,
			hemangioendothelioma,
			angiosarcoma,
			haemangiopericytoma,
			lymphangioma,
			lymphangiosarcoma. Highly
	-		preferred indications also
			include cancers such as,
			prostate, breast, lung, colon,
			pancreatic, esophageal,
			stomach, brain, liver, and
			urinary cancer. Preferred

indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications	also include arterial disease, such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s disease and Reynaud"s	phenomenom, aneurysms, restenosis; venous and lymphatic disorders such as thrombophlebitis, lymphangitis, and lymphangitis, and lymphedema; and other	vascular disorders such as peripheral vascular disease, and cancer. Highly preferred indications also include trauma such as wounds, burns, and injured	tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury,

cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and
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111000		Exemplary assays that may be	blockage), seizures, mental
		used or routinely modified to	confusion, drowsiness,
		test for stimulation of insulin	nonketotic hyperglycemic-
		secretion (from pancreatic	hyperosmolar coma,
		cells) by polypeptides of the	cardiovascular disease (e.g.,
		invention (including antibodies	heart disease, atherosclerosis,
		and agonists or antagonists of	microvascular disease,
		the invention) include assays	hypertension, stroke, and other
		disclosed in: Ahren, B., et al.,	diseases and disorders as
		Am J Physiol, 277(4 Pt	described in the
		2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
		al., Endocrinology,	section below), dyslipidemia,
		138(9):3735-40 (1997); Kim,	endocrine disorders (as
		K.H., et al., FEBS Lett,	described in the "Endocrine
		377(2):237-9 (1995); and,	Disorders" section below),
		Miraglia S et. al., Journal of	neuropathy, vision impairment
		Biomolecular Screening,	(e.g., diabetic retinopathy and
		4:193-204 (1999), the contents	blindness), ulcers and impaired
		of each of which is herein	wound healing, and infection
		incorporated by reference in its	(e.g., infectious diseases and
		entirety. Pancreatic cells that	disorders as described in the
		may be used according to these	"Infectious Diseases" section
		assays are publicly available	below, especially of the
		(e.g., through the ATCC)	urinary tract and skin), carpal
		and/or may be routinely	tunnel syndrome and
		generated. Exemplary	Dupuytren's contracture).
		pancreatic cells that may be	An additional highly preferred
		used according to these assays	indication is obesity and/or
		include rat INS-1 cells. INS-1	complications associated with
		cells are a semi-adherent cell	obesity. Additional highly
		line established from cells	preferred indications include

isolated from an X-ray induced weight loss or alternatively, rat transplantable insulinoma.  These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992	1152 SEAP in Jurkat/IL4 promoter	79 Hexosaminidase in RBL-2H3	79 IL-8 in SW480	79 1152 SEAP in SW480	1153 Activation of Kinase assay. JNK and p38	Cell kinase assays for signal	Doo of JINK   Transduction that regulate cell   Includes a method for   Signaling Pathway.   Proliferation activation or   Stimulating endothelial cell	apoptosis are well known in	 routinely modified to assess invention includes a method	-	the ability of polypeptides of for inhibiting endothelial cell		 				
						End E-20	psg   Sign	<b>b</b>					<u> </u>	<u> </u>		<u> </u>	
	HFVAB79 1	HFVAB79 1	HFVAB79 1	HFVAB79 1	HFVGE32			¥0, 44,									
	204	204	204	204		205									-		

	for JNK and p38 kinase	of the invention includes a
	activity that may be used or	method for inhibiting
	routinely modified to test JNK	endothelial cell proliferation.
	and p38 kinase-induced	A highly preferred
	activity of polypeptides of the	embodiment of the invention
	invention (including antibodies	includes a method for
	and agonists or antagonists of	stimulating apoptosis of
	the invention) include the	endothelial cells. An
	assays disclosed in Forrer et	alternative highly preferred
-	al., Biol Chem 379(8-9):1101-	embodiment of the invention
	1110 (1998); Gupta et al., Exp	includes a method for
	Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
 4	(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
	Soc Symp 64:29-48 (1999);	A highly preferred
	Chang and Karin, Nature	embodiment of the invention
	410(6824):37-40 (2001); and	includes a method for
	Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
	the contents of each of which	alternative highly preferred
	are herein incorporated by	embodiment of the invention
	reference in its entirety.	includes a method for
	Endothelial cells that may be	inhibiting (e.g., decreasing) the
	used according to these assays	activation of and/or
	are publicly available (e.g.,	inactivating endothelial cells.
	through the ATCC).	A highly preferred
	Exemplary endothelial cells	embodiment of the invention
	that may be used according to	includes a method for
	these assays include human	stimulating angiogenisis. An
	umbilical vein endothelial cells	alternative highly preferred
	(HUVEC), which are	embodiment of the invention
	endothelial cells which line	includes a method for

inhibiting angiogenesis. A highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,
venous blood vessels, and are involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.																									
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1 1 1 1 1 1 1 1	disorders (e.g. systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly
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preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal,	stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such	as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease,	such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s disease and Reynaud"s phenomenom, aneurysms, restenosis; venous and	lymphatic disorders such as thrombophlebitis, lymphangitis, and lymphedema; and other vascular disorders such as	peripheral vascular disease, and cancer. Highly preferred indications also include trauma such as wounds, burns, and injured tissue (e.g., vascular injury
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such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury,	rheumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis. Additional highly preferred	indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph	angiogenesis, sexual disorders, age-related macular degeneration, and treatment /prevention of endometriosis and related conditions.	indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease.  Preferred indications include	blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders").
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					Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain
206	HFVIC62	1154	SEAP in HIB/CRE		management.
206	HFVIC62	1154	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-

		the ability of nolyneptides of	Related Disorders", and/or
		the invention (including	"Cardiovascular Disorders").
		antibodies and agonists or	Preferred indications include
		antagonists of the invention) to	autoimmune diseases (e.g.,
		regulate GATA3 transcription	rheumatoid arthritis, systemic
		factors and modulate	lupus erythematosis, multiple
		expression of mast cell genes	sclerosis and/or as described
		important for immune response	below) and
		development. Exemplary	immunodeficiencies (e.g., as
		assays for transcription	described below). Preferred
		through the GATA3 response	indications include neoplastic
_		element that may be used or	diseases (e.g., leukemia,
		routinely modified to test	lymphoma, melanoma,
		GATA3-response element	prostate, breast, lung, colon,
		activity of polypeptides of the	pancreatic, esophageal,
		invention (including antibodies	stomach, brain, liver, and
		and agonists or antagonists of	urinary tract cancers and/or as
		the invention) include assays	described below under
		disclosed in Berger et al., Gene	"Hyperproliferative
		66:1-10 (1998); Cullen and	Disorders"). Other preferred
		Malm, Methods in Enzymol	indications include benign
		216:362-368 (1992); Henthorn	dysproliferative disorders and
		et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
		85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
		et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
		Quant Biol 64:563-571 (1999);	Preferred indications include
		Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
		J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
		(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
		Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
	•	Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,

				14(6):4286-4294 (1994), the contents of each of which are	multiple myeloma, Burkitt's lymphoma, arthritis. AIDS.
				herein incorporated by	granulomatous disease,
				reference in its entirety. Mast	inflammatory bowel disease,
				cells that may be used	sepsis, neutropenia,
				according to these assays are	neutrophilia, psoriasis,
				publicly available (e.g.,	suppression of immune
				through the ATCC).	reactions to transplanted
				Exemplary human mast cells	organs and tissues, hemophilia,
				that may be used according to	hypercoagulation, diabetes
				these assays include the HMC-	mellitus, endocarditis,
				1 cell line, which is an	meningitis, and Lyme Disease.
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HFVIC62	1154	Activation of	This reporter assay measures	Highly preferred indications
206			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
•				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
				response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-

Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g.,	rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma,	prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and	urnnary tract cancers and/or as described below under "Hyperproliferative Disorders"). Other preferred indications include benign	dysproliterative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.  Preferred indications include	anemia, pancytopenia, leukopenia, thrombocytopenia, leukemias, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas,
used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes	involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that	may be used or routinely modified to test NFAT-response element activity of	polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthom et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); De Boer	et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Ali et al., J Immunol 165(12):7215-7223 (2000); Hutchinson and McCloskey, J
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			Biol Chem 270(27):16333-16338 (1995), and Turner et al., J Exp Med 188:527-537 (1998), the contents of each of which are herein incorporated by reference in its entirety.  Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes melitus, endocarditis, meningitis, and Lyme Disease.
HFXAM76	1155	Production of GM-CSF	Immature mast cells.  GM-CSF FMAT. GM-CSF is expressed by activated T cells, macrophages, endothelial cells, and fibroblasts. GM-CSF regulates differentiation and proliferation of granulocytes-macrophage progenitors and enhances antimicrobial activity in neutrophils, monocytes and macrophage. Additionally, GM-CSF plays an important	A highly preferred embodiment of the invention includes a method for stimulating the production of GM-CSF. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of GM-CSF. Highly preferred indications include inflammation and

role in the differentiation of dendritic cells and monocytes, additional highly preferred and increases antigen presentation. GM-CSF is described below under considered to be a "Infectious Disease."	ytokine. omodulatory ote the -CSF are art and may	evaluate the production of evaluate the production of cytokines, such as GM-CSF, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention)

				·	pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel
					disease, sepsis, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and allergy.
HFXDJ75	3775	1156	Activation of	Assays for the activation of	Preferred indications
			transcription	transcription through the AP1	include neoplastic diseases
			response element in	known in the art and may be	"Hyperproliferative
			immune cells (such	used or routinely modified to	Disorders"), blood disorders
			as T-cells).	assess the ability of	(e.g., as described below under
				polypeptides of the invention	"Immune Activity",
				(including antibodies and	"Cardiovascular Disorders",
		·		agonists or antagonists of the	and/or "Blood-Related
				invention) to modulate growth	Disorders"), and infection
				and other cell functions.	(e.g., an infectious disease as
				Exemplary assays for	described below under
				transcription through the AP1	"Infectious Disease"). Highly
				response element that may be	preferred indications include
				used or routinely modified to	autoimmune diseases (e.g.,
				test AP1-response element	rheumatoid arthritis, systemic
				activity of polypeptides of the	lupus erythematosis, multiple
				invention (including antibodies	sclerosis and/or as described

	and agonists or antagonists of	below) and
	the invention) include assays	imminodeficiencies (e g. as
	the invention include assays	decomination to term Additional
	disclosed in Berger et al., Gene	described below). Additional
	 66:1-10 (1988); Cullen and	highly preferred indications
	Malm, Methods in Enzymol	include inflammation and
	216:362-368 (1992); Henthorn	inflammatory disorders.
	et al., Proc Natl Acad Sci USA	Highly preferred indications
	85:6342-6346 (1988);	also include neoplastic
	Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
	 272(49):30806-30811 (1997);	lymphoma, and/or as described
-	Chang et al., Mol Cell Biol	below under
	18(9):4986-4993 (1998); and	"Hyperproliferative
	Fraser et al., Eur J Immunol	Disorders"). Highly preferred
	29(3):838-844 (1999), the	indications include neoplasms
	contents of each of which are	and cancers, such as, leukemia,
	herein incorporated by	lymphoma, prostate, breast,
	reference in its entirety.	lung, colon, pancreatic,
	Human T cells that may be	esophageal, stomach, brain,
	 used according to these assays	liver, and urinary cancer. Other
	are publicly available (e.g.,	preferred indications include
	through the ATCC).	benign dysproliferative
	Exemplary human T cells that	disorders and pre-neoplastic
	may be used according to these	conditions, such as, for
	assays include the SUPT cell	example, hyperplasia,
	line, which is an IL-2 and IL-4	metaplasia, and/or dysplasia.
	responsive suspension-culture	Preferred indications include
	cell line.	arthritis, asthma, AIDS,
		allergy, anemia, pancytopenia,
		leukopenia, thrombocytopenia,
 		Hodgkin's disease, acute
		lymphocytic anemia (ALL),

					plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis,
208	HFXDJ75	1156	Activation of transcription through CD28 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of	A highly preferred embodiment of the invention stimulating T cell proliferation. An alternative highly preferred embodiment of the invention
				polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to test CD28-response element	includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for includes a method for includes a method for inhibiting the activation of
				activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and	and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-2 production. An alternative

highly preferred embodiment of the invention includes a method for inhibiting (e o	reducing) IL-2 production.	Additional nightly preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below),	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune	response, and suppressing a T	cell-mediated immune	response. Highly preferred	indications include neoplastic	diseases (e.g., melanoma, renal	cell carcinoma, leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, melanoma (e.g.,	metastatic melanoma), renal
Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al. Proc Natl Acad Sci USA	85:6342-6346 (1988);	Integrate and Iacobelli, J Immunol 159(3):1319-1327	(1997); Parra et al., J Immunol	166(4):2437-2443 (2001); and	Butscher et al., J Biol Chem	3(1):552-560 (1998), the	contents of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the SUPT cell	line, which is a suspension	culture of IL-2 and IL-4	responsive T cells.								
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	renal cell carcinoma),
	leukemia, lymphoma (e.g., T
	cell lymphoma), and prostate,
	breast, lung, colon, pancreatic,
	esophageal, stomach, brain,
	liver and urinary cancer. Other
	preferred indications include
	benign dysproliferative
	disorders and pre-neoplastic
	conditions, such as, for
	example, hyperplasia,
	metaplasia, and/or dysplasia.
	A highly preferred indication
	includes infection (e.g.,
	AIDS, tuberculosis, infections
	associated with granulomatous
	disease, and osteoporosis,
	and/or as described below
	under "Infectious Disease").
	highly preferred indication is
-	AIDS. Additional highly
	preferred indications include
	suppression of immune
	reactions to transplanted
	organs and/or tissues, uveitis,
	psoriasis, and tropical spastic
	paraparesis. Preferred
	indications include blood
	disorders (e.g., as described
	pelow under "Immune

Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis,
	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes.
	Activation of transcription through NFKB response element in immune cells (such as T-cells).
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	HFXDJ75
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multiple sclerosis and/or as	described below), and	immunodeficiencies (e.g., as	described below). An	additional highly preferred	indication is infection (e.g.,	AIDS, and/or an infectious	disease as described below	under "Infectious Disease").	Highly preferred indications	include neoplastic diseases	(e.g., melanoma, leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such	as,melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also
Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Black et	al., Virus Gnes 15(2):105-117	(1997); and Fraser et al.,	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the SUPT cell	line, which is a suspension	culture of IL-2 and IL-4
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				responsive T cells.	include anemia, pancytopenia,
					leukopenia, thrombocytopenia, Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					inyelolina, burklit s tympnolina, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					suppression of immune
					reactions to transplanted
Ī					organs, asthma and allergy.
	HFXDN63	1157	Activation of	Assays for the activation of	A preferred embodiment of
			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related

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Disorders", and/or "Cardiovascular Disorders")	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma.
function of growth-related genes in many cell types.	Exemplary assays for	transcription through the SRE	that may be used or routinely	modified to test SRE activity	of the polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,	which is a human natural killer	cell line with cytolytic and
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melanoma, glioma (e.g.,	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and	acthma and allerov An
cytotoxic activity.																													
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additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays
	Production of ICAM-1
	1158
	HFXGT26
	010

				-	
				include microvascular endothelial cells (MVEC).	
11	HFXGV31	1159	Production of TNF	TNFa FMAT. Assays for	A highly preferred
117			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
_			cells	produced by activated	includes a method for
				macrophages, T cells,	inhibiting (e.g., decreasing)
-	-			fibroblasts, smooth muscle,	TNF alpha production. An
			,	and other cell types that exert a	alternative highly preferred
				wide variety of inflammatory	embodiment of the invention
				and cytotoxic effects on a	includes a method for
				variety of cells are well known	stimulating (e.g., increasing)
				in the art and may be used or	TNF alpha production.
				routinely modified to assess	Highly preferred indications
				the ability of polypeptides of	include blood disorders (e.g.,
				the invention (including	as described below under
				antibodies and agonists or	"Immune Activity", "Blood-
				antagonists of the invention) to	Related Disorders", and/or
				mediate immunomodulation,	"Cardiovascular Disorders"),
	·			modulate inflammation and	Highly preferred indications
				cytotoxicity. Exemplary	include autoimmune diseases
·				assays that test for	(e.g., rheumatoid arthritis,
				immunomodulatory proteins	systemic lupus erythematosis,
				evaluate the production of	Crohn"s disease, multiple
				cytokines such as tumor	sclerosis and/or as described
				necrosis factor alpha (TNFa),	below), immunodeficiencies
				and the induction or inhibition	(e.g., as described below),
				of an inflammatory or	boosting a T cell-mediated
				cytotoxic response. Such	immune response, and
				assays that may be used or	suppressing a T cell-mediated
				routinely modified to test	immune response. Additional
				immunomodulatory activity of	highly preferred indications

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				and functional activities.	lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
212	HFXHD88	1160	CD152 in Human T cells		
213	HFXHK73	1161	Activation of Adipocyte ERK Signaling Pathway		A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A
				invention (including antibodies	highly preferred embodiment

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of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for	inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment of the invention includes a	activation of (e.g., decreasing) and/or inactivating adipocytes. Highly preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders"). Highly preferred indications also include neoplastic diseases (e.g., lipomas, liposarcomas, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include blood disorders (e.g., hypertension.
and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be	used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel V, Exp. Clin	Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC).

congestive heart failure, blood vessel blockage, heart disease, stroke, impotence and/or as described below under	"Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under	"Immune Activity"), neural disorders (e.g., as described below under "Neural Activity and Neurological Diseases"), and infection (e.g., as	described below under "Infectious Disease"). A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication	associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other	described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic
Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1	is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and	undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.			

neuropathy), blood vessel	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with
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obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications and	complications associated with insulin resistance.  Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as	described herein.  Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia,	and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver and uringer concer.

Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	1161 IgG in Human B cells	1162 IgG in Human B cells SAC	Transcription transcription are well-known in the art and may be used and routinely modified to assess ability of polypeptides of the invention to inhibit or activate transcription. An example of such an assay follows: Cells were pretreated with SID supernatants or controls for 15-18 hours. SEAP activity was measured after 48 hours.  LSI74T is an epithelial colon adenocarcinoma cell line. Its tumourigenicity in nude mice make cell line LS174T a model
	1161	1162	1162
	HFXHK73	HFXKJ03	HFXKJ03
	213	214	214

				colon cancer. See, Patan et al.,	
				Circ Kes, 89(8):/32-39 (2001),	
				the contents of which are	
				herein incorporated by	
				reference in its entirety.	
	HFXKJ03	1162	Activation of	Assays for the activation of	A preferred embodiment of
214			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
	-			regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
				genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
				transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,
				of the polypeptides of the	Crohn"s disease, multiple
				invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below), immunodeficiencies
				the invention) include assays	(e.g., as described below),
				disclosed in Berger et al., Gene	boosting a T cell-mediated
				66:1-10 (1998); Cullen and	immune response, and

suppressing a T cell-mediated horn immune response. Additional highly preferred indications son include inflammation and			and/or as described below under "Hyperproliferative Disorders"). Additionally			esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic	conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117	which are herein incorporated by reference in its entirety. T cells that may be used	according to these assays are publicly available (e.g., through the ATCC).	used according to these assays include the NK-YT cell line, which is a human natural killer	cell line with cytolytic and cytotoxic activity.		

				Preferred indications include
				anemia, pancytopenia,
				leukopenia, thrombocytopenia,
-				Hodgkin's disease, acute
				lymphocytic anemia (ALL),
				plasmacytomas, multiple
	_			myeloma, Burkitt's lymphoma,
				arthritis, AIDS, granulomatous
				disease, inflammatory bowel
				disease, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted
-				organs and tissues, hemophilia,
				hypercoagulation, diabetes
				mellitus, endocarditis,
<del>-</del>	***			meningitis, Lyme Disease,
				cardiac reperfusion injury, and
				asthma and allergy. An
				additional preferred indication
		MLL.		is infection (e.g., an infectious
				disease as described below
				under "Infectious Disease").
HFXKT05	1163	Myoblast cell	Assays for muscle cell	Highly preferred indications
		proliferation	proliferation are well known in	include diabetes, myopathy,
			the art and may be used or	muscle cell atrophy, cancers of
			routinely modified to assess	muscle (such as,
			the ability of polypeptides of	rhabdomyoma, and
			the invention (including	rhabdosarcoma),
			antibodies and agonists or	cardiovascular disorders (such
			antagonists of the invention) to	as congestive heart failure.

cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart disease, cardiac arrest, heart valve disease, vascular disease, and	also as described below under "Cardiovascular Disorders"), stimulating myoblast	myoblast proliferation.				
stimulate or inhibit myoblast cell proliferation. Exemplary assays for myoblast cell proliferation that may be used or routinely modified to test	activity of polypeptides and antibodies of the invention (including agonists or antagonists of the invention)	include, for example, assays disclosed in: Soeta, C., et al. "Possible role for the c-ski	gene in the proliferation of myogenic cells in regenerating skeletal muscles of rats" Dev Growth Differ Apr;43(2):155-	64 (2001); Ewton DZ, et al., "IGF binding proteins-4, -5 and -6 may play specialized roles during L6 myoblast	differentiation" J Endocrinol Mar;144(3):539-53 (1995); and, Pampusch MS, et al., Effect of transforming	growth factor beta on proliferation of L6 and embryonic porcine myogenic cells" J Cell Physiol Jun;143(3):524-8 (1990); the contents of each of which are

	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte inhibiting adipocyte inhibiting adipocyte inhibiting adipocyte
herein incorporated by reference in their entirety.  Exemplary myoblast cells that may be used according to these assays include the rat myoblast L6 cell line. Rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation media.	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell stransduction that regulate cell stransduction or differentiation pare well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies hin and agonists or antagonists of the invention) to promote or inhibit cell proliferation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to intest ERK kinase-induced
	Activation of Adipocyte ERK Signaling Pathway
ı	1164
	HFXKY27
	1446

preferred embodiment of the invention includes a method for stimulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment	of the invention includes a method for inhibiting the activation of (e.g., decreasing)	Highly preferred indications include endocrine disorders	(e.g., as described below under "Endocrine Disorders"). Highly preferred indications	also include neoplastic diseases (e.g., lipomas, liposarcomas, and/or as	described below under "Hyperproliferative Disorders"). Preferred	indications include blood disorders (e.g., hypertension, congestive heart failure, blood vessel blockage heart disease	stroke, impotence and/or as described below under "Immune Activity",	"Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders
activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al. Biol Chem 370(8-0):1101.	Brustel Y, Exp Clin Endocrinol Diabetes	107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang	410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by	reference in its entirety.  Mouse adipocyte cells that may be used according to these	assays are publicly available (e.g., through the ATCC).  Exemplary mouse adipocyte cells that may be used	according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse	preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed

- th	through clonal isolation and	(e.g., as described below under
<u>n</u>	undergo a pre-adipocyte to	"Immune Activity"), neural
	adipose-like conversion under	disorders (e.g., as described
la de la	appropriate differentiation	below under "Neural Activity
<u> </u>	conditions known in the art.	and Neurological Diseases"),
		and infection (e.g., as
		described below under
		"Infectious Disease").
		A highly preferred indication
		is diabetes mellitus. An
		additional highly preferred
 		indication is a complication
 		associated with diabetes (e.g.,
		diabetic retinopathy, diabetic
		nephropathy, kidney disease
		(e.g., renal failure,
-		nephropathy and/or other
		diseases and disorders as
		described in the "Renal
		Disorders" section below),
		diabetic neuropathy, nerve
		disease and nerve damage
		(e.g., due to diabetic
		neuropathy), blood vessel
		blockage, heart disease, stroke,
		impotence (e.g., due to diabetic
		neuropathy or blood vessel
		blockage), seizures, mental
		confusion, drowsiness,
		nonketotic hyperglycemic-
		hyperosmolar coma,

cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred
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indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. Preferred	indications include neoplasms	and cancer, such as,	Iymphoma, leukemia and	breast, colon, and kidney	cancer. Additional preferred	indications include melanoma,	prostate, lung, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer.	Highly preferred indications	include lipomas and	liposarcomas. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.
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				-																					, and a second		- Production of	******		

	HFXKY27	1164	Activation of	Assays for the activation of	Highly preferred indications
			transcription	transcription through the	include neoplastic diseases
			through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
_			response element in	Site (GAS) response element	and/or as described below
			immune cells (such	are well-known in the art and	under "Hyperproliferative
			as T-cells).	may be used or routinely	Disorders"). Highly preferred
				modified to assess the ability	indications include neoplasms
				of polypeptides of the	and cancers, such as, for
				invention (including antibodies	example, leukemia, lymphoma
				and agonists or antagonists of	(e.g., T cell lymphoma,
				the invention) to regulate	Burkitt's lymphoma, non-
				STAT transcription factors and	Hodgkins lymphoma,
				modulate gene expression	Hodgkin"s disease),
	-			involved in a wide variety of	melanoma, and prostate,
				cell functions. Exemplary	breast, lung, colon, pancreatic,
				assays for transcription	esophageal, stomach, brain,
				through the GAS response	liver and urinary cancer. Other
				element that may be used or	preferred indications include
				routinely modified to test	benign dysproliferative
				GAS-response element activity	disorders and pre-neoplastic
				of polypeptides of the	conditions, such as, for
				invention (including antibodies	example, hyperplasia,
				and agonists or antagonists of	metaplasia, and/or dysplasia.
				the invention) include assays	Preferred indications include
				disclosed in Berger et al., Gene	autoimmune diseases (e.g.,
				66:1-10 (1998); Cullen and	rheumatoid arthritis, systemic
				Malm, Methods in Enzymol	lupus erythematosis, multiple
				216:362-368 (1992); Henthorn	sclerosis and/or as described
				et al., Proc Natl Acad Sci USA	below), immunodeficiencies
	31.21			85:6342-6346 (1988);	(e.g., as described below),
				Matikainen et al., Blood	boosting a T cell-mediated

immune response, and suppressing a T cell-mediated immune response. Additional preferred indications include inflammation and	inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under	"Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral	infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant	osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis.	Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease,
93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by	reference in its entirety.  Exemplary mouse T cells that may be used according to these assays are publicly available	(e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the CTLL cell line,	which is a suspension culture of IL-2 dependent cytotoxic T cells.		

sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.			Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Vascular Disease, Atherosclerosis, Restenosis, Stroke, and Asthma.
			Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Rolfe BE, et al., Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365 (1995); and, Grunstein MM, et
	Glucose Production in H4IIE	IgG in Human B cells	Production of ICAM-1
	1164	1164	1165
	HFXKY27	HFXKY27	HGBFO79
	216	216	217

HGBFO79
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below under "Infectious Disease"), autoimmune diseases (e.g., rheumatoid	arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and	immunodeficiencies (e.g., as described below).			
Madison, WI, USA ) can be used to measure the number of viable cells in culture based on	quantitation of the ATP present which signals the presence of metabolically active cells. Mast cells are	found in connective and mucosal tissues throughout the body. Mast cell activation (via immunoglobulin E -antigen,	promoted by T helper cell type 2 cytokines) is an important component of allergic disease. Dysregulation of mast cell apoptosis may play a role in	allergic disease and mast cell tumor survival. Mast cell lines that may be used according to these assays are publicly available and/or may be routinely generated.  Exemplary mast cells that may	be used according to these assays include HMC-1, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.

and coding  and coding  be specific sterol  ly. See l. Chem. (993), the re herein  re treated  nts, and measured oG2 is a  ar (ATCC owles et al., (1980), the re herein re herein re herein		ation of Highly preferred indications include blood disorders (e.g., as described below under mse element "Immune Activity", "Blood-	
Reporter Assay: construct contains regulatory and coding sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its entirety.		Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element	
Inhibition of squalene synthetase gene transcription.	CD71 in Human T cells	Activation of transcription through NFAT response element in	immune cells (such as natural killer cells).
1166	1166	1167	
HGBHE57	HGBHE57	HGBIB74	
218	218	219	

	immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune	response, and suppressing a real-mediated immune response. Additional highly preferred indications include	inflammatory disorders. An additional highly preferred indication is infection (e.g., an infectious disease as described	below under "Infectious Disease"). Preferred indications include neoplastic diseases (e.g., leukemia,	lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms	and cancers, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred
8 9	involved in immunomodulatory functions.	transcription through the NFAT response element that may be used or routinely	response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the	invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol	216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De	Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993),
		7. wi y 1 <u>se</u>				
			·			

				the contents of each of which	indications include benign
				are herein incorporated by	dysproliferative disorders and
				reference in its entirety. NK	pre-neoplastic conditions, such
				cells that may be used	as, for example, hyperplasia,
				according to these assays are	metaplasia, and/or dysplasia.
				publicly available (e.g.,	Preferred indications also
	-	·		through the ATCC).	include anemia, pancytopenia,
				Exemplary human NK cells	leukopenia, thrombocytopenia,
				that may be used according to	Hodgkin's disease, acute
				these assays include the NK-	lymphocytic anemia (ALL),
				YT cell line, which is a human	plasmacytomas, multiple
				natural killer cell line with	myeloma, Burkitt's lymphoma,
				cytolytic and cytotoxic	arthritis, AIDS, granulomatous
				activity.	disease, inflammatory bowel
					disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
,	HGBIB74	1167	Activation of	Assays for the activation of	A preferred embodiment of
219			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,

anti	antibodies and agonists or	increasing) TNF alpha
ant	antagonists of the invention) to	production. Preferred
 reg	regulate serum response	indications include blood
fact	factors and modulate the	disorders (e.g., as described
exp	expression of genes involved	below under "Immune
gni	in growth and upregulate the	Activity", "Blood-Related
unj	function of growth-related	Disorders", and/or
l gen	genes in many cell types.	"Cardiovascular Disorders"),
Exe	Exemplary assays for	Highly preferred indications
tran	transcription through the SRE	include autoimmune diseases
that	that may be used or routinely	(e.g., rheumatoid arthritis,
ош	modified to test SRE activity	systemic lupus erythematosis,
oft	of the polypeptides of the	Crohn"s disease, multiple
vari	invention (including antibodies	sclerosis and/or as described
and	and agonists or antagonists of	below), immunodeficiencies
 the	the invention) include assays	(e.g., as described below),
disc	disclosed in Berger et al., Gene	boosting a T cell-mediated
:99	66:1-10 (1998); Cullen and	immune response, and
Maj	Malm, Methods in Enzymol	suppressing a T cell-mediated
216	216:362-368 (1992); Henthorn	immune response. Additional
eta	et al., Proc Natl Acad Sci USA	highly preferred indications
85:0	85:6342-6346 (1988); Benson	include inflammation and
eta	et al., J Immunol 153(9):3862-	inflammatory disorders, and
387	3873 (1994); and Black et al.,	treating joint damage in
Vir	Virus Genes 12(2):105-117	patients with rheumatoid
(19	(1997), the content of each of	arthritis. An additional highly
whi	which are herein incorporated	preferred indication is sepsis.
by 1	by reference in its entirety. T	Highly preferred indications
cell	cells that may be used	include neoplastic diseases
acc	according to these assays are	(e.g., leukemia, lymphoma,
qnd	publicly available (e.g.,	and/or as described below

under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example,	leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid	lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other	preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for	example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia,	Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted
through the ATCC).  Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer	cell line with cytolytic and cytotoxic activity.					

organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").		Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, non-Hodgkins lymphoma, non-Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative
		Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test
	SEAP in NK16/STAT6	Activation of transcription through GAS response element in immune cells (such as T-cells).
	1167	1167
	HGBIB74	HGBIB74
	219	219

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disorders and pre-neoplastic conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an	infectious disease as described
GAS-response element activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary human T cells,	such as the SUPT cell line, that	may be used according to these	assays are publicly available	(e.g., through the ATCC).								
											-																		
		-																											
						4710																							

below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha
	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to
	Activation of transcription through serum response element in immune cells (such as T-cells).
	1168
	HGLAL82
·	220

	regulate the serum response	esponse	indications include blood
	factors and modulate the	e the	disorders (e.g., as described
	expression of genes involved	involved	below under "Immune
	in growth. Exemplary assays	ary assays	Activity", "Blood-Related
	for transcription through the	ough the	Disorders", and/or
	SRE that may be used or	ed or	"Cardiovascular Disorders"),
	routinely modified to test SRE	to test SRE	Highly preferred indications
	activity of the polypeptides of	eptides of	include autoimmune diseases
	the invention (including	ding	(e.g., rheumatoid arthritis,
	antibodies and agonists or	ists or	systemic lupus erythematosis,
	antagonists of the invention)	nvention)	Crohn"s disease, multiple
	include assays disclosed in	osed in	sclerosis and/or as described
	Berger et al., Gene 66:1-10	66:1-10	below), immunodeficiencies
,	(1998); Cullen and Malm,	Malm,	(e.g., as described below),
	Methods in Enzymol 216:362-	ol 216:362-	boosting a T cell-mediated
	368 (1992); Henthorn et al.,	rn et al.,	immune response, and
	Proc Natl Acad Sci USA	USA	suppressing a T cell-mediated
-	85:6342-6346 (1988); and	8); and	immune response. Additional
	Black et al., Virus Genes	Jenes	highly preferred indications
	12(2):105-117 (1997), the	7), the	include inflammation and
	content of each of which are	which are	inflammatory disorders, and
	herein incorporated by	by	treating joint damage in
	reference in its entirety.	rety. T	patients with rheumatoid
	cells that may be used	eq	arthritis. An additional highly
	according to these assays are	issays are	preferred indication is sepsis.
	publicly available (e.g.,	e.g.,	Highly preferred indications
	through the ATCC).		include neoplastic diseases
	Exemplary mouse T cells that	cells that	(e.g., leukemia, lymphoma,
	may be used according to these	ing to these	and/or as described below
	assays include the CTLL cell	CTLL cell	under "Hyperproliferative
	line, which is an IL-2	-2	Disorders"). Additionally,

highly preferred indications include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,
dependent suspension culture of T cells with cytotoxic	activity.																										### Proc. 1		
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diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").		Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal assay, for ERK signal transduction that regulate cell proliferation or differentiation of polypeptides of the modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or includes a method for simulating natural killer cell proliferation, and differentiation. An alternative highly preferred embodiment of the invention activation, and differentiation. An alternative highly preferred embodiment of the invention woulfied to say says for ERK kinase activity that may be includes a method for inhibiting natural killer cell differentiation. Highly activity of polypeptides of the preferred indications include	ī/O
	IL-13 in HMC	Activation of Kinase Natural Killer Cell for exa ERK Signaling transdy prolife are we may be modificated by the invention of polyments and age the invention inhibit activat Exemptical control of polyministic activat Exemptical control of polyministic activat Exemptical control of polyministic activat activat activity activity activity activity	inventi
	1169	1169	
ī	HHAAF20	HHAAF20	
	221	221	

the invention) include the assays disclosed in Forrer et al., Biot Chan 370(92); 1011–101 (1998); Kriakis JM, Biochem Soc Symp 64:29-48  (1999); Chang and Karin, and Cobb MH, Prog (2001); and Cobb MH, Prog (2001); and Cobb MH, Prog (e.g., sa described below under Biophys Mol Biol 71(3-4)-479. "Immune Activity" and 500 (1999); the contents of incietions (e.g., sa described each of white was be used according to these assays are publicly the canner bloow under "Infections and ATCC. Exemplary manual Discuse"). Preferred entirety. Natural killer cells indications include blood these assays are publicly according to these assays are publicly according to these assays include the human natural include and entirest order the human natural killer cells that may be used according to these assays include the human antaral killer cell with may be used according to these assays include the human natural include and inflammatory disorders. Activity and extirity or primary NK cells which have cyclopytic and cytotoxic multiple sclerosis and/or a described below). Additional highly preferred indications include inflammation and inflammatical and in the programmatical and in the programmatical and in the programmatical and in the programmatical and in the progr																													
the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MI, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Natural killer cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary natural killer cell that may be used according to these assays include the human natural killer cell lines (for example, NK-YT cells which have cytolytic and cytotoxic activity) or primary NK cells.	"Hyperproliferative Disorders"), blood disorders	(e.g., as described below under "Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity") and	infections (e.g., as described	below under "Infectious	Disease"). Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Highly preferred indications	also include cancers such as
	assays disclosed in Forrer et	al., blot Chem 379(8-9):1101- 1110 (1998); Kyriakis JM,	Biochem Soc Symp 64:29-48	(1999); Chang and Karin,	Nature 410(6824):37-40	(2001); and Cobb MH, Prog	Biophys Mol Biol 71(3-4):479-	500 (1999); the contents of	each of which are herein	incorporated by reference in its	entirety. Natural killer cells	that may be used according to	these assays are publicly	available (e.g., through the	ATCC). Exemplary natural	killer cells that may be used	according to these assays	include the human natural	killer cell lines (for example,	NK-YT cells which have	cytolytic and cytotoxic	activity) or primary NK cells.							
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				kidney, melanoma, prostate,
				breast, lung, colon, pancreatic,
				esophageal, stomach, brain,
				liver, urinary cancer,
				lymphoma and leukemias.
				Other preferred indications
				include benign dysproliferative
				disorders and pre-neoplastic
				conditions, such as, for
				example, hyperplasia,
				metaplasia, and/or dysplasia.
				Other highly preferred
				indications include,
				pancytopenia, leukopenia,
				leukemias, Hodgkin's disease,
				acute lymphocytic anemia
				(ALL), arthritis, asthma,
				AIDS, granulomatous disease,
				inflammatory bowel disease,
				sepsis, psoriasis, immune
				reactions to transplanted
				organs and tissues,
				endocarditis, meningitis, Lyme
			1000	Disease, and allergies.
HHBCS39	1170	Activation of	Kinase assay. Kinase assays,	A highly preferred
		Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
		Signaling Pathway	assay, for ERK signal	includes a method for
			transduction that regulate cell	stimulating adipocyte
			proliferation or differentiation	proliferation. An alternative
			are well known in the art and	highly preferred embodiment
			may be used or routinely	of the invention includes a

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method for inhibiting	adipocyte proliferation. A	highly preferred embodiment	of the invention includes a	method for stimulating	adipocyte differentiation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting adipocyte	differentiation. A highly	preferred embodiment of the	invention includes a method	for stimulating (e.g.,	increasing) adipocyte	activation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting the	activation of (e.g., decreasing)	and/or inactivating adipocytes.	Highly preferred indications	include endocrine disorders	(e.g., as described below under	"Endocrine Disorders").	Highly preferred indications	also include neoplastic	diseases (e.g., lipomas,	liposarcomas, and/or as	described below under	"Hyperproliferative
modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to promote or	inhibit cell proliferation,	activation, and differentiation.	Exemplary assays for ERK	kinase activity that may be	used or routinely modified to	test ERK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Le Marchand-	Brustel Y, Exp Clin	Endocrinol Diabetes	107(2):126-132 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Mouse adipocyte cells that
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may be used according to these
assays are publicly available
(e.g., through the ATCC).
Exemplary mouse adipocyte
cells that may be used
according to these assays
include 3T3-L1 cells. 3T3-L1
is an adherent mouse
preadipocyte cell line that is a
continuous substrain of 3T3
fibroblast cells developed
through clonal isolation and
undergo a pre-adipocyte to
adipose-like conversion under
appropriate differentiation
conditions known in the art.

diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke,	impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-	cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other	diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine	Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing infection (e.g.	infectious diseases and disorders as described in the "Infectious Diseases" section below (particularly of the urinary tract and skin). An
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additional highly preferred indication is obesity and/or	complications associated with	obesity. Additional nighty preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. Preferred	indications include neoplasms	and cancer, such as,	lymphoma, leukemia and	breast, colon, and kidney	cancer. Additional preferred	indications include melanoma,
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		<del></del>	<del></del> -						•		<del></del>												<del></del>					
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	<u> </u>															-		_						<del></del>				
													14	72														

prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	SEAP in HIB/CRE	170 TNFa in Human T-cell 2B9	Activation of Kinase assay. Kinase assays,	for example an Elk-1 kinase		 	and	modified to assess the ability   method for inhibiting	 invention (including antibodies   highly preferred embodiment	and agonists or antagonists of of the invention includes a	the invention) to promote or method for stimulating	inhibit cell proliferation, adipocyte differentiation. An	activation, and differentiation.   alternative highly preferred	Exemplary account for FRK embodiment of the invention
	1170 SE	1170 TN cell	1171 Act	Ad	Sig									
	HHBCS39	HHBCS39	HHEAA08											
	222	222	223	677									-	

	used or routinely modified to	inhihiting adinocyte
	test FRK kinase-induced	differentiation A highly
	activity of nolynentides of the	
	activity of polypopules of tile	preferred enrocument of the
	invention (including antibodies	invention includes a method
	and agonists or antagonists of	for stimulating (e.g.,
	the invention) include the	increasing) adipocyte
	assays disclosed in Forrer et	activation. An alternative
	al., Biol Chem 379(8-9):1101-	highly preferred embodiment
	1110 (1998); Le Marchand-	of the invention includes a
	Brustel Y, Exp Clin	method for inhibiting the
	Endocrinol Diabetes	activation of (e.g., decreasing)
	107(2):126-132 (1999);	and/or inactivating adipocytes.
	Kyriakis JM, Biochem Soc	Highly preferred indications
	Symp 64:29-48 (1999); Chang	include endocrine disorders
	and Karin, Nature	(e.g., as described below under
	410(6824):37-40 (2001); and	"Endocrine Disorders").
	Cobb MH, Prog Biophys Mol	Highly preferred indications
	Biol 71(3-4):479-500 (1999);	also include neoplastic
	the contents of each of which	diseases (e.g., lipomas,
	are herein incorporated by	liposarcomas, and/or as
	reference in its entirety.	described below under
	Mouse adipocyte cells that	"Hyperproliferative
	may be used according to these	Disorders"). Preferred
	assays are publicly available	indications include blood
	(e.g., through the ATCC).	disorders (e.g., hypertension,
	Exemplary mouse adipocyte	congestive heart failure, blood
	cells that may be used	vessel blockage, heart disease,
	according to these assays	stroke, impotence and/or as
	include 3T3-L1 cells. 3T3-L1	described below under
	is an adherent mouse	"Immune Activity",
0.000	preadipocyte cell line that is a	"Cardiovascular Disorders",

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and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), neural	disorders (e.g., as described	below under "Neural Activity	and Neurological Diseases"),	and infection (e.g., as	described below under	"Infectious Disease").	A highly preferred indication	is diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	Confinion duringing
continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	conditions known in the art.			10.0																					
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nonketotic hyperglycemic- hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease,	hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as	Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section	below (particularly of the urinary tract and skin). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with

insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems	including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery	gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms	and cancer, such as, Iymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications	include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such

as, for example, hyperplasia, metaplasia, and/or dysplasia.						
					RANTES FMAT. Assays for immunomodulatory proteins that induce chemotaxis of T cells, monocytes, and eosinophils are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and/or mediated immunity.  Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as RANTES, and the induction of	chemotactic responses in
	CD152 in Human T cells	RANTES in Human T cells	IL-5 in Th2	IL-6 in HUVEC	Production of RANTES in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))	
	1171	1171	1171	1172	1172	
	HHEAA08	HHEAA08	HHEAA08	HHEMA59	ННЕМА59	
	223	223	223	224	75	

immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Cocchi et al., Science	270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp	Immunol 101(3):398-407	(1995), the contents of each of	which are herein incorporated	by reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line	venous blood vessels, and are
	-																		-											11.

				involved in functions that	
				include, but are not limited to,	
				angrogenesis, vasculai permeability vascular tone	
				and immune cell extravasation.	
	HHEMA59	1172	Activation of	Assays for the activation of	A preferred embodiment of
224			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
_			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
				genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
				transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,
				of the polypeptides of the	Crohn's disease, multiple
				invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below), immunodeficiencies
				the invention) include assays	(e.g., as described below),
				disclosed in Berger et al., Gene	boosting a T cell-mediated
				66:1-10 (1998); Cullen and	immune response, and

	Malm Methods in Enzymol	Suppressing a T coll-madiated
-	716:369-368 (1007): Hantham	immino concessor Additional
	210:302-308 (1322), Hellulolli	iniliule response. Additional
	et al., Proc Natl Acad Sci USA	highly preferred indications
	85:6342-6346 (1988); Benson	include inflammation and
	et al., J Immunol 153(9):3862-	inflammatory disorders, and
	3873 (1994); and Black et al.,	treating joint damage in
	Virus Genes 12(2):105-117	patients with rheumatoid
	(1997), the content of each of	arthritis. An additional highly
	which are herein incorporated	preferred indication is sepsis.
	by reference in its entirety. T	Highly preferred indications
	cells that may be used	include neoplastic diseases
	according to these assays are	(e.g., leukemia, lymphoma,
	publicly available (e.g.,	and/or as described below
	through the ATCC).	under "Hyperproliferative
	Exemplary T cells that may be	Disorders"). Additionally,
	used according to these assays	highly preferred indications
	include the NK-YT cell line,	include neoplasms and
	 which is a human natural killer	cancers, such as, for example,
	cell line with cytolytic and	leukemia, lymphoma,
	 cytotoxic activity.	melanoma, glioma (e.g.,
		malignant glioma), solid
		tumors, and prostate, breast,
		lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver and urinary cancer. Other
		preferred indications include
		benign dysproliferative
		disorders and pre-neoplastic
		conditions, such as, for
		example, hyperplasia,
		metaplasia, and/or dysplasia.

					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
•					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
<u>.</u>					suppression of immune
•					reactions to transplanted
_					organs and tissues, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
	HHEMA75	1173	Activation of	Assays for the activation of	Preferred indications include
			transcription	transcription through the	blood disorders (e.g., as
			through cAMP	cAMP response element are	described below under
			response element in	well-known in the art and may	"Immune Activity", "Blood-
			immune cells (such	be used or routinely modified	Related Disorders", and/or
-			as T-cells).	to assess the ability of	"Cardiovascular Disorders"),
				polypeptides of the invention	and infection (e.g., an
				(including antibodies and	infectious disease as described

agonists or antagonists of the	below under "Infectious
invention) to increase cAMP,	Disease"). Preferred
bind to CREB transcription	indications include
factor, and modulate	autoimmune diseases (e.g.,
expression of genes involved	rheumatoid arthritis, systemic
in a wide variety of cell	lupus erythematosis, multiple
functions. Exemplary assays	sclerosis and/or as described
for transcription through the	below), immunodeficiencies
cAMP response element that	(e.g., as described below),
may be used or routinely	boosting a T cell-mediated
modified to test cAMP-	immune response, and
response element activity of	suppressing a T cell-mediated
polypeptides of the invention	immune response. Additional
(including antibodies and	preferred indications include
agonists or antagonists of the	inflammation and
 invention) include assays	inflammatory disorders.
disclosed in Berger et al., Gene	Highly preferred indications
66:1-10 (1998); Cullen and	include neoplastic diseases
Malm, Methods in Enzymol	(e.g., leukemia, lymphoma,
216:362-368 (1992); Henthorn	and/or as described below
et al., Proc Natl Acad Sci USA	under "Hyperproliferative
85:6342-6346 (1988); Black et	Disorders"). Highly preferred
al., Virus Genes 15(2):105-117	indications include neoplasms
(1997); and Belkowski et al., J	and cancers, such as, leukemia,
Immunol 161(2):659-665	lymphoma (e.g., T cell
(1998), the contents of each of	lymphoma, Burkitt's
which are herein incorporated	lymphoma, non-Hodgkins
by reference in its entirety. T	lymphoma, Hodgkin"s
cells that may be used	disease), melanoma, and
according to these assays are	prostate, breast, lung, colon,
publicly available (e.g.,	pancreatic, esophageal.

				through the ATCC).	stomach, brain, liver and
				Exemplary human T cells that	urinary cancer. Other preferred
				may be used according to these	indications include benign
				assays include the JURKAT	dysproliferative disorders and
				cell line, which is a suspension	pre-neoplastic conditions, such
				culture of leukemia cells that	as, for example, hyperplasia,
				produce IL-2 when stimulated.	metaplasia, and/or dysplasia.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					acute lymphocytic anemia
		••			(ALL), plasmacytomas,
					multiple myeloma, arthritis,
					AIDS, granulomatous disease,
					inflammatory bowel disease,
		-			sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
		1414			reactions to transplanted
		·			organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, and
					asthma and allergy.
ļ	HHEMA75	1173	SEAP in Jurkat/IL4		
577			promoter		
	HHEMA75	1173	Activation of	Assays for the activation of	Highly preferred indications
225			transcription	transcription through the	include blood disorders (e.g.,
			through NFAT	Nuclear Factor of Activated T	as described below under
			response element in	cells (NFAT) response element	"Immune Activity", "Blood-
			immune cells (such	are well-known in the art and	Related Disorders", and/or

	as natural killer	may be used or routinely	"Cardiovascular Disorders").
-	cells).	modified to assess the ability	Highly preferred indications
		of polypeptides of the	include autoimmune diseases
		invention (including antibodies	(e.g., rheumatoid arthritis,
		and agonists or antagonists of	systemic lupus erythematosis,
		the invention) to regulate	multiple sclerosis and/or as
		NFAT transcription factors and	described below),
		modulate expression of genes	immunodeficiencies (e.g., as
		involved in	described below), boosting a T
		immunomodulatory functions.	cell-mediated immune
		Exemplary assays for	response, and suppressing a T
		transcription through the	cell-mediated immune
		NFAT response element that	response. Additional highly
		may be used or routinely	preferred indications include
	•	modified to test NFAT-	inflammation and
		response element activity of	inflammatory disorders. An
		polypeptides of the invention	additional highly preferred
		(including antibodies and	indication is infection (e.g., an
		agonists or antagonists of the	infectious disease as described
-		invention) include assays	below under "Infectious
121		disclosed in Berger et al., Gene	Disease"). Preferred
		66:1-10 (1998); Cullen and	indications include neoplastic
		Malm, Methods in Enzymol	diseases (e.g., leukemia,
,		216:362-368 (1992); Henthorn	lymphoma, and/or as described
		et al., Proc Natl Acad Sci USA	below under
		85:6342-6346 (1988);	"Hyperproliferative
		Aramburu et al., J Exp Med	Disorders"). Preferred
		182(3):801-810 (1995); De	indications include neoplasms
		Boer et al., Int J Biochem Cell	and cancers, such as, for
		Biol 31(10):1221-1236 (1999);	example, leukemia, lymphoma,
		Fraser et al., Eur J Immunol	and prostate, breast, lung,

				29(3):838-844 (1999); and	colon, pancreatic, esophageal,
				Yeseen et al., J Biol Chem	stomach, brain, liver and
				268(19):14285-14293 (1993),	urinary cancer. Other preferred
				the contents of each of which	indications include benign
_	_			are herein incorporated by	dysproliferative disorders and
				reference in its entirety. NK	pre-neoplastic conditions, such
				cells that may be used	as, for example, hyperplasia,
				according to these assays are	metaplasia, and/or dysplasia.
				publicly available (e.g.,	Preferred indications also
				through the ATCC).	include anemia, pancytopenia,
			-	Exemplary human NK cells	leukopenia, thrombocytopenia,
				that may be used according to	Hodgkin's disease, acute
				these assays include the NK-	lymphocytic anemia (ALL),
				YT cell line, which is a human	plasmacytomas, multiple
				natural killer cell line with	myeloma, Burkitt's lymphoma,
				cytolytic and cytotoxic	arthritis, AIDS, granulomatous
				activity.	disease, inflammatory bowel
_					disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
		-			suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
	HHFMA75	1173	SEAD in		asunna and anergy.
225			NK16/STAT6		
	HHEMA75	1173	Activation of	Assays for the activation of	Preferred indications
225			transcription	transcription through the AP1	include neoplastic diseases
		<b></b>	through AP1	response element are well-	(e.g., as described below under

response element in	known in the art and may be	"Hyperproliferative
	used or routinely modified to	Disorders"), blood disorders
as T-cells).	assess the ability of	(e.g., as described below under
	polypeptides of the invention	"Immune Activity",
	(including antibodies and	"Cardiovascular Disorders",
	agonists or antagonists of the	and/or "Blood-Related
	invention) to modulate growth	Disorders"), and infection
	and other cell functions.	(e.g., an infectious disease as
	Exemplary assays for	described below under
	transcription through the AP1	"Infectious Disease"). Highly
	response element that may be	preferred indications include
	used or routinely modified to	autoimmune diseases (e.g.,
 	test AP1-response element	rheumatoid arthritis, systemic
	activity of polypeptides of the	lupus erythematosis, multiple
	invention (including antibodies	sclerosis and/or as described
	and agonists or antagonists of	below) and
	the invention) include assays	immunodeficiencies (e.g., as
	disclosed in Berger et al., Gene	described below). Additional
	66:1-10 (1988); Cullen and	highly preferred indications
	Malm, Methods in Enzymol	include inflammation and
	216:362-368 (1992); Henthorn	inflammatory disorders.
	et al., Proc Natl Acad Sci USA	Highly preferred indications
	85:6342-6346 (1988);	also include neoplastic
	Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
	272(49):30806-30811 (1997);	lymphoma, and/or as described
	Chang et al., Mol Cell Biol	below under
	18(9):4986-4993 (1998); and	"Hyperproliferative
	Fraser et al., Eur J Immunol	Disorders"). Highly preferred
	29(3):838-844 (1999), the	indications include neoplasms
	contents of each of which are	and cancers, such as, leukemia,
	herein incorporated by	lymphoma, prostate, breast,

				reference in its entirety.	lung, colon, pancreatic.
				Human T cells that may be	esophageal, stomach, brain,
				used according to these assays	liver, and urinary cancer. Other
-				are publicly available (e.g.,	preferred indications include
				through the ATCC).	benign dysproliferative
-				Exemplary human T cells that	disorders and pre-neoplastic
				may be used according to these	conditions, such as, for
				assays include the SUPT cell	example, hyperplasia,
				line, which is an IL-2 and IL-4	metaplasia, and/or dysplasia.
-				responsive suspension-culture	Preferred indications include
_				cell line.	arthritis, asthma, AIDS,
					allergy, anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression of
					immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
206	HHEMA/5	1173	Activation of	Assays for the activation of	A highly preferred
C77			transcription	transcription through the CD28	embodiment of the invention
			through CD28	response element are well-	includes a method for
			response element in	known in the art and may be	stimulating T cell proliferation.
			immune cells (such	used or routinely modified to	An alternative highly preferred
			as T-cells).	assess the ability of	embodiment of the invention
				polypeptides of the invention	includes a method for

		(including antibodies and	inhibiting T cell proliferation.
		agonists or antagonists of the	A highly preferred
		invention) to stimulate IL-2	embodiment of the invention
		expression in T cells.	includes a method for
	198	Exemplary assays for	activating T cells. An
		transcription through the CD28	alternative highly preferred
		response element that may be	embodiment of the invention
		used or routinely modified to	includes a method for
		test CD28-response element	inhibiting the activation of
		activity of polypeptides of the	and/or inactivating T cells.
		invention (including antibodies	A highly preferred
		and agonists or antagonists of	embodiment of the invention
		the invention) include assays	includes a method for
-		disclosed in Berger et al., Gene	stimulating (e.g., increasing)
		66:1-10 (1998); Cullen and	IL-2 production. An alternative
		Malm, Methods in Enzymol	highly preferred embodiment
-		216:362-368 (1992); Henthorn	of the invention includes a
		et al., Proc Natl Acad Sci USA	method for inhibiting (e.g.,
		 85:6342-6346 (1988);	reducing) IL-2 production.
		McGuire and Iacobelli, J	Additional highly preferred
		Immunol 159(3):1319-1327	indications include
		(1997); Parra et al., J Immunol	inflammation and
		166(4):2437-2443 (2001); and	inflammatory disorders.
		Butscher et al., J Biol Chem	Highly preferred indications
		3(1):552-560 (1998), the	include autoimmune diseases
		contents of each of which are	(e.g., rheumatoid arthritis,
		herein incorporated by	systemic lupus erythematosis,
		reference in its entirety. T	multiple sclerosis and/or as
		cells that may be used	described below),
		according to these assays are	immunodeficiencies (e.g., as
		 publicly available (e.g.,	described below), boosting a T

		through the ATCC).	cell-mediated immune
		Exemplary human T cells that	response, and suppressing a T
		may be used according to these	cell-mediated immune
		assays include the SUPT cell	response. Highly preferred
		line, which is a suspension	indications include neoplastic
-		culture of IL-2 and IL-4	diseases (e.g., melanoma, renal
		responsive T cells.	cell carcinoma, leukemia,
			lymphoma, and/or as described
			below under
			"Hyperproliferative
			Disorders"). Highly preferred
	-		indications include neoplasms
			and cancers, such as, for
			example, melanoma (e.g.,
			metastatic melanoma), renal
-			cell carcinoma (e.g., metastatic
			renal cell carcinoma),
			leukemia, lymphoma (e.g., T
			cell lymphoma), and prostate,
			breast, lung, colon, pancreatic,
			esophageal, stomach, brain,
			liver and urinary cancer. Other
-			preferred indications include
			benign dysproliferative
			disorders and pre-neoplastic
			conditions, such as, for
			example, hyperplasia,
			metaplasia, and/or dysplasia.
			A highly preferred indication
			includes infection (e.g.,
<u>.</u>			AIDS, tuberculosis, infections

associated with granulomatous disease, and osteoporosis, and/or as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly	preferred indications include suppression of immune reactions to transplanted	organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood	disorders (e.g., as described below under "Immune Activity", "Blood-Related	Disorders", and/or "Cardiovascular Disorders"). Preferred indications also	include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute	lymphocyuc anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, granulomatous	disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes
	-						

					meningitis, Lyme Disease,
	HHEMA75	1173	Activation of	Assays for the activation of	Highly preferred indications
225			transcription	transcription through the	include neoplastic diseases
			through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
_			response element in	Site (GAS) response element	and/or as described below
			immune cells (such	are well-known in the art and	under "Hyperproliferative
			as T-cells).	may be used or routinely	Disorders"). Highly preferred
				modified to assess the ability	indications include neoplasms
				of polypeptides of the	and cancers, such as, for
	_			invention (including antibodies	example, leukemia, lymphoma
				and agonists or antagonists of	(e.g., T cell lymphoma,
				the invention) to regulate	Burkitt's lymphoma, non-
-				STAT transcription factors and	Hodgkins lymphoma,
				modulate gene expression	Hodgkin's disease),
				involved in a wide variety of	melanoma, and prostate,
				cell functions. Exemplary	breast, lung, colon, pancreatic,
_				assays for transcription	esophageal, stomach, brain,
_				through the GAS response	liver and urinary cancer. Other
				element that may be used or	preferred indications include
				routinely modified to test	benign dysproliferative
				GAS-response element activity	disorders and pre-neoplastic
				of polypeptides of the	conditions, such as, for
				invention (including antibodies	example, hyperplasia,
				and agonists or antagonists of	metaplasia, and/or dysplasia.
_				the invention) include assays	Preferred indications include
				disclosed in Berger et al., Gene	autoimmune diseases (e.g.,
				66:1-10 (1998); Cullen and	rheumatoid arthritis, systemic
				Malm, Methods in Enzymol	lupus erythematosis, multiple
	-			216:362-368 (1992); Henthorn	sclerosis and/or as described
				et al., Proc Natl Acad Sci USA	below), immunodeficiencies

(e.g., as described below), boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an	infectious disease as described	below under "Infectious	Disease"). An additional	preferred indication is	idiopathic pulmonary fibrosis.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, arthritis,
85:6342-6346 (1988); Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary human T cells,	such as the SUPT cell line, that	may be used according to these	assays are publicly available	(e.g., through the ATCC).															-			
					-																								
																													;
																													_

AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	Assays for the activation of transcription through the cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies invention) to regulate modulate expression of genes involved in munomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely include autoimmune diseases invention) to regulate and agonists or antagonists of and agonists or antagonists of e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly may be used or routinely inflammation and
	Activation of transcription transcription transponse element in ce immune cells (such ar as T-cells).    m as T-cells).   m of in
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	225

response element activity of	inflammatory disorders. An
polypeptides of the invention	additional highly preferred
 (including antibodies and	indication is infection (e.g., an
agonists or antagonists of the	infectious disease as described
invention) include assays	below under "Infectious
 disclosed in Berger et al., Gene	Disease"). Preferred
66:1-10 (1998); Cullen and	indications include neoplastic
Malm, Methods in Enzymol	diseases (e.g., leukemia,
216:362-368 (1992); Henthorn	lymphoma, and/or as described
et al., Proc Natl Acad Sci USA	below under
85:6342-6346 (1988); Serfling	"Hyperproliferative
et al., Biochim Biophys Acta	Disorders"). Preferred
1498(1):1-18 (2000); De Boer	indications include neoplasms
et al., Int J Biochem Cell Biol	and cancers, such as, for
31(10):1221-1236 (1999);	example, leukemia, lymphoma,
Fraser et al., Eur J Immunol	and prostate, breast, lung,
29(3):838-844 (1999); and	colon, pancreatic, esophageal,
Yeseen et al., J Biol Chem	stomach, brain, liver and
268(19):14285-14293 (1993),	urinary cancer. Other preferred
the contents of each of which	indications include benign
are herein incorporated by	dysproliferative disorders and
reference in its entirety. T	pre-neoplastic conditions, such
cells that may be used	as, for example, hyperplasia,
according to these assays are	metaplasia, and/or dysplasia.
publicly available (e.g.,	Preferred indications also
through the ATCC).	include anemia, pancytopenia,
Exemplary human T cells that	leukopenia, thrombocytopenia,
may be used according to these	Hodgkin's disease, acute
assays include the SUPT cell	lymphocytic anemia (ALL),
line, which is a suspension	plasmacytomas, multiple
culture of IL-2 and IL-4	myeloma, Burkitt's lymphoma,

		(including antibodies and	disease as described below
		agonists or antagonists of the	under "Infectious Disease").
		invention) include assays	Highly preferred indications
		disclosed in Berger et al., Gene	include neoplastic diseases
	~.	66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
		Malm, Methods in Enzymol	lymphoma, and/or as described
		216:362-368 (1992); Henthorn	below under
		et al., Proc Natl Acad Sci USA	"Hyperproliferative
		85:6342-6346 (1988); Black et	Disorders"). Highly preferred
		al., Virus Gnes 15(2):105-117	indications include neoplasms
		(1997); and Fraser et al.,	and cancers, such
	<del>/</del>	29(3):838-844 (1999), the	as,melanoma, renal cell
		contents of each of which are	carcinoma, leukemia,
		herein incorporated by	lymphoma, and prostate,
		reference in its entirety. T	breast, lung, colon, pancreatic,
		cells that may be used	esophageal, stomach, brain,
		according to these assays are	liver and urinary cancer. Other
		publicly available (e.g.,	preferred indications include
		through the ATCC).	benign dysproliferative
	******	Exemplary human T cells that	disorders and pre-neoplastic
		may be used according to these	conditions, such as, for
		assays include the SUPT cell	example, hyperplasia,
		line, which is a suspension	metaplasia, and/or dysplasia.
		culture of IL-2 and IL-4	Preferred indications also
		responsive T cells.	include anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			Hodgkin's disease, acute
			lymphocytic anemia (ALL),
			plasmacytomas, multiple
			myeloma, Burkitt's lymphoma,
			arthritis, AIDS,

					granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and alleroy.
526	HHEMM /4	4/11	Activation of transcription through cAMP response element in immune cells (such as T-cells).	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP and regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. Exemplary assays for transcription	Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies
				through the cAMP response element that may be used or routinely modified to test cAMP-response element activity of polypeptides of the	(e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional

			invention (including antibodies and agonists or antagonists of	preferred indications include inflammation and
			the invention) include assays	inflammatory disorders.
			disclosed in Berger et al., Gene	Highly preferred indications
			66:1-10 (1998); Cullen and	include neoplastic diseases
			Malm, Methods in Enzymol	(e.g., leukemia, lymphoma,
			216:362-368 (1992); Henthorn	and/or as described below
			et al., Proc Natl Acad Sci USA	under "Hyperproliferative
	•		85:6342-6346 (1988); Black et	Disorders"). Highly preferred
			al., Virus Genes 15(2):105-117	indications include neoplasms
			(1997); and Belkowski et al., J	and cancers, such as, for
	-		Immunol 161(2):659-665	example, leukemia, lymphoma
			(1998), the contents of each of	(e.g., T cell lymphoma,
			which are herein incorporated	Burkitt's lymphoma, non-
			 by reference in its entirety. T	Hodgkins lymphoma,
			cells that may be used	Hodgkin"s disease),
			according to these assays are	melanoma, and prostate,
			publicly available (e.g.,	breast, lung, colon, pancreatic,
			through the ATCC).	esophageal, stomach, brain,
			Exemplary mouse T cells that	liver and urinary cancer. Other
			may be used according to these	preferred indications include
			assays include the CTLL cell	benign dysproliferative
			line, which is a suspension	disorders and pre-neoplastic
-			culture of IL-2 dependent	conditions, such as, for
			cytotoxic T cells.	example, hyperplasia,
				metaplasia, and/or dysplasia.
				Preferred indications include
				anemia, pancytopenia,
		***************************************		leukopenia, thrombocytopenia,
				acute lymphocytic anemia
				(ALL), plasmacytomas,

multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g. as
AIDS, a inflamr sepsis, neutrop suppres reaction organs hemoph diabetes mening asthma	A highl embodi include stimular IL-6 pro highly pof the inmethod reducin highly preferre blood describe "Immun Related "Cardio and infe
	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced lgE production and increases lgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth
	Production of IL-6
	1175
	HHENQ22
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